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THE SURGICAL TREATMENT OF PARKINSONISM

BY

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[WITH SPECIAL PLATE]

Until recent years the surgical treatment of Parkinsonism has been largely confined to interruption of the cortico-spinal pathways at various levels: at the cerebral cortex, internal capsule, cerebral peduncle, and spinal cord. The results of these different procedures and their associated morbidity were not encouraging, and the physiological basis of their application was not sufficiently secure to inspire confidence in the pursuit of the problem in this way.

Russell Myers, of New York (1942), changed the direction of our thinking by the observation that operative interruption of the pallidofugal fibres might modify rigidity and tremor in patients with Parkinsonism. His open operative approach, through the corpus callosum and third ventricle, was formidable and necessarily hazardous. Nevertheless, the early results indicated that his basic concept was correct.

Fénélon, of Paris (1950), described an improved approach using a subfrontal route to the anterior perforated substance, interrupting the ansa lenticularis immediately above the termination of the optic tract by a thermal lesion, using electrocoagulation. The results were promising, and his method was adopted by Guiot and Brion (1953) and others, including ourselves, with conspicuous success.

In the meantime Spiegel *et al.* (1947) had described the first stereotaxic apparatus for operations on the human brain. In so doing they laid the foundations for the development of this type of surgery, with corresponding reduction in mortality and morbidity. Others, notably Talairach *et al.* (1952) in Paris, Leksell (1949) in Lund, Riechert (1954) in Freiburg, Cooper (1955) in New York, Guiot (1958) in Paris, and Bertrand (1958) in Montreal, each developed their own stereotaxic technique. The accumulating information from these various operative procedures has supported Myers's original concept and observations. It would now seem that the strategic interruption of the pallidofugal fibres is an effective surgical means for the alleviation of rigidity and tremor in Parkinsonism, and the involuntary movements of some of the dyskinesias.

Present Study

The evolution of the surgical treatment of the disease in Edinburgh began in March, 1955. This paper is therefore concerned with the study, over a period of five years, of the effect of thermal electrocoagulation lesions in the globus pallidus, internal capsule, and thalamus, separately or in combination, in 60 patients with Parkinsonism. Each was systematically assessed, and the findings were recorded before treatment in respect of neurological and intellectual functions and emotional state by the neurosurgeon, neurologist, and medical psychologist of the team. Similar detailed studies were made during and after operation. The surgeon and radiologist were jointly responsible for the combined surgical and radiological procedures, and for the plotting of the site and extent of the lesion on stereotaxic anatomical charts, in each case. The charts were first based on the atlas of Spiegel and Wycis (1952), and latterly on that of Schaltenbrand and Bailey (1959). Finally, an extended follow-up along these lines of up to five years, and not less than nine months, has been carried out, embodying the reports of the patient, a close relative, and the attending general practitioner.

The 60 patients were all under 65, except one, a man of 72, with strictly unilateral disease. The largest group were between the ages of 50 and 60. There was no selection of cases apart from imposing an upper age limit of 65. Before considering treatment, investigations were carried out to exclude the possibility of further medical or other surgical means of treatment—for example, hepato-lenticular degeneration and brain tumour.

Our first two patients, both with unilateral left-sided Parkinsonism, were treated by interruption of the ansa lenticularis and globus pallidus by electrocoagulation, using the open subfrontal route described by Fénélon. Both patients were greatly benefited and showed no morbidity. Two months after operation they returned to work, and have subsequently maintained their improvement over the years. One of them with post-encephalitic Parkinsonism was so disabled that he was unable to work for ten years before operation five years ago, and was confined to bed for some period of each week because of increased rigidity, tremor, inertia, malaise, and sweating. These features of his illness disappeared after operation.

The open operative procedure, however satisfactory in these two patients, is exacting under local anaesthesia and has obvious hazards (Gillingham, 1958). Because of this we soon followed a simple stereotaxic method based on that described by Guiot (1958). The remaining 58 patients have therefore been treated in this way since

April, 1957, with considerable development of the apparatus and its method of application over the past three years. We feel that the merits of this method lie in the relatively short operative procedure and in its accuracy and simplicity. Its principles are based on the fact that the globus pallidus and thalamus bear a reasonably constant anatomical relationship to the anterior and posterior commissures, the intercommissural line, and the mid-sagittal plane of the head (Spiegel and Wycis, 1952; Housepian and Carpenter, 1957).

Radiological and Operative Techniques

The operative procedure is carried out in two stages. These are normally separated by an interval of at least 48 hours, but sometimes in very disabled patients we have waited two weeks. The first stage, under general or local anaesthesia, determines the mid-sagittal plane of the brain, the position of the anterior and posterior commissures, and the length of the intercommissural line.

With the patient supine and later prone, three short scalp incisions are made and a series of radio-opaque markers (lead shot) are inserted into the outer table of the skull in holes made with a small dental burr 1 mm. apart. These markers are placed astride the mid-line of the skull at three points: at the upper margin of the frontal sinus, at the coronal suture, and 5 cm. above the external occipital protuberance. Exposure of the coronal and lambdoid sutures and their junction with the interparietal suture gives an approximate guide to the mid-sagittal plane. In addition, a right frontal burr-hole is made 2–3 cm. from the mid-line at the level of the coronal suture. Through it a rubber catheter is passed into the frontal horn of the lateral ventricle for the insertion of radio-opaque "myodil" (ethyl iodophenylundecylate) at the second stage. If the second stage of the operation is purposely delayed the catheter is not inserted. The wounds are sutured and the patient is seated erect.

Lumbar pneumoencephalography is immediately carried out, using about 25 c.cm. of air. It is important to obtain a good lateral erect film in order to demonstrate the posterior commissure. The anterior commissure may also be visible on the lateral erect film. Further films are obtained in the supine position. The lateral supine film, the neck being extended if necessary, shows the anterior commissure. The posterior view is of great importance and must be obtained in the true sagittal plane. This is best achieved by exposing one film in what is judged to be the correct position, together with another two, the *x*-ray tube being shifted a few degrees to either side. One of these three films is usually satisfactory.

The lead markers corresponding to the mid-sagittal plane of the brain, as judged by the position of the septum pellucidum and the third ventricle, are chosen and recorded. Then the wounds are reopened, and the selected markers are removed and replaced by special stainless-steel screws, the heads of which are recessed to accommodate the pins of the stereotaxic frame. These screws are left in permanently. The wounds are closed and the patient is returned to the ward (Special Plate, Fig. 1).

The second stage is usually carried out 48 hours later, under local anaesthesia in order that the patient's co-operation can be obtained and his reactions observed. Minimal sedation is given, yet patients tolerate the procedure very well and co-operate to the full.

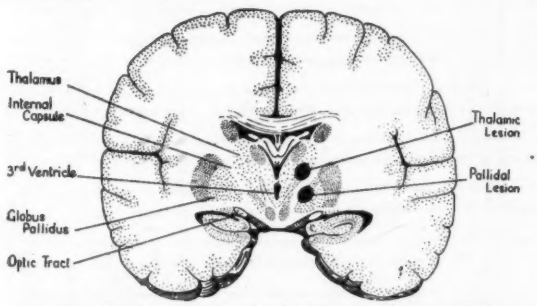
The patient is first placed on his side and the pins of the stereotaxic frame are inserted through the sutured wounds into the heads of the three special screws (Special Plate, Fig. 2). He is then turned into the prone position, the cheeks being supported in a special face-rest and the image amplifier moved into position on either side of the head. About 6 ml. of myodil is injected through the ventricular catheter inserted at the first stage, or through a brain cannula. The frontal horn is filled until the contrast medium just spills over into the anterior part of the third ventricle and outlines the anterior commissure. The minimum quantity of contrast medium compatible with the clear demonstration of this landmark is advised, though much can be removed at the end of operation. In our experience reactions have been very few and temporary in any case. The injection of the myodil is controlled fluoroscopically by the use of the image amplifier.

Next the transverse bar or cursor is applied to the stereotaxic frame posteriorly, its optimum position on the frame having been determined already from the *x*-ray film obtained at the first stage (Special Plate, Fig. 3). The sights attached to the cursor can then be aligned opposite the target point in the globus pallidus. For practical purposes this is a constant point 3 mm. posterior to the posterior margin of the anterior commissure and 1 mm. below the intercommissural line. The adjustment of the sights into the correct position is controlled fluoroscopically by the radiologist using the image amplifier. Provided that the target is kept strictly in the centre of the field of the image amplifier, *x*-ray distortion can be neglected. An *x*-ray film of the correctly aligned sights is usually taken, and while this is being processed the surgeon makes a burr-hole in the occipital region immediately beneath the electrode guide tube (Special Plate, Fig. 4). The guide tube is usually fixed at 16 mm. from the mid-line, but enlargement of the third ventricle increases this measurement proportionally, especially at the level of the globus pallidus.

The length of the electrode to be inserted is measured against the sights, and it is passed gently through the occipital lobe and across the lateral ventricle. Its contact with the pulvinar of the thalamus can be felt clearly, and the distance between it and the target point in the globus pallidus measured. The electrode is gently pushed on through the ependyma into the thalamus to a point calculated to be at the junction of the internal capsule and thalamus. Confirmation that the tip of the electrode lies in the ventro-lateral nucleus of the thalamus adjacent to the internal capsule is usually evident on stimulation or with low-output coagulation, the patient experiencing a tingling sensation in the contralateral side, usually at the angle of the mouth and over the thumb and index finger. At the higher voltages of stimulation between 5 and 8 volts, or if the electrode lies more anterior in the capsule, there may be involuntary movement of fingers, wrist, and arm, or, if more anterior still, of the face. Movement or disturbance of sensation in the contralateral lower limb is unusual at this distance from the mid-line, occurring in more lateral positions (Guiot, 1959).

When the surgeon and radiologist are satisfied with the correct siting of the electrode, electrocoagulation is carried out over periods of five seconds, and its intensity

increased from a low to a predetermined level according to the size of the lesion required (usually 7 by 5 by 5 mm.). Tremor is often damped down during the period of stimulation, and indeed sometimes disappears with the insertion of the electrode into the thalamus. Coagulation usually abolishes tremor and lessens rigidity. There is, in addition, colour change, the hand becoming pink and less puffy as compared with a somewhat cyanosed, puffy limb with marked venous distension. Motor contractions or paraesthesiae with low coagulation suggest malplacement of the electrode, and it should be readjusted until these cease. Finally the electrode is gently passed across the internal capsule to its final target point in the globus pallidus. As it crosses the capsule and enters the globus pallidus there is a further, and often complete, loss of rigidity and restoration of facility of movement in the contralateral limbs. Stimulation at this point usually causes no subjective sensation to the patient (occasionally he may see a poorly localized flash of light with higher voltages). Electrocoagulation is then carried out as before, creating a lesion of similar volume to that in the thalamus (see Diagram). Intractable pain, which is sometimes associated with rigidity, decreases with the creation of the thalamic lesion, and disappears altogether with the further pallidal lesion. Depth recording with the standard electrode in a few patients has been relatively unfruitful.



Showing situation of lesions in thalamus and globus pallidus.

The electrode is withdrawn and gently replaced by a similar instrument with a detachable tip along the same track. The tip is a stainless-steel ball 1.5 mm. in diameter, and when detached marks the anterior margin of the lesion. The instrument is withdrawn and the stereotaxic apparatus removed. Finally, the wounds are closed in layers after withdrawing myodil and removing the ventricular catheter. The stainless-steel screws remain in the skull and are used for subsequent treatment of the other hemisphere in patients with bilateral Parkinsonism.

Immediate post-operative radiographs are taken without moving the patient, to determine the position of the marker in relation to the anterior commissure, the intercommissural line, and the sagittal plane. No movement of the marker has been noted at this early stage, and we have felt secure in using it as a basis for charting the lesions. After some weeks or months it has been shown to move a little (less than 5 mm.), probably within an area of coagulation necrosis (Special Plate, Fig. 5), or possibly within a cystic cavity, or back along the track. We have observed no ill-effects from its retention.

In charting our lesions we have been fully aware of an individual variation of the basal ganglia to the commissures, the internal capsule, and to one another. The co-ordinates used from the beginning of this study were the anterior and posterior commissures, the intercommissural line, and from August, 1958, the addition of a vertical line drawn from the mid-point. Subsequent charting of the lesions on the atlas of Schaltenbrand and Bailey has consequently been a simple matter (Special Plate, Fig. 6). Individual variations have been partly overcome by relating the length of the intercommissural line, and latterly the distance between the anterior commissure and pulvinar, in each patient to those measurements of the standard brain of the atlas (Brierley and Beck, 1957). The probable size of our electrocoagulation lesions was determined from studies on fresh necropsy material, and calibration of our diathermy apparatus was done in this way. These estimations have been confirmed by the careful study of three patients who died some time after operative treatment.

In every patient active physiotherapy was started one week after operation. Most patients began to get up and about on the third post-operative day. Attention was particularly paid to posture and walking and to the rehabilitation of the improved limbs. Some patients showed a tendency to neglect the improved limbs temporarily. There were no sensory deficits to account for this. No doubt the disabled limb had been neglected for some time pre-operatively because of uselessness from gross disability, but this cannot be accepted as the whole explanation.

Analysis of Results

The results are considered in Tables I to IV. In Table I each patient is presented chronologically according to the date of his or her first operation. The various columns of the table show the individual pre-operative state, the results of operations, and the particular lesions made in achieving these results. Suitable grading scales have been used in the columns, and these are explained in the table and its footnotes. It is necessary, however, to regroup the patients in order to analyse the results further, and this is done with the aid of Tables II, III, and IV.

In Table II the 60 patients have been divided into three broad pre-operative groups, for it is impossible to assess the results of any method of surgical treatment for Parkinsonism unless the pre-operative severity and extent of the condition are known exactly in the sample of cases under discussion. In the first group, 19 patients had rigidity and tremor almost entirely confined to the limbs on one side of the body, and there was little or no other evidence of Parkinsonism. In the second group, 24 patients were afflicted with bilateral limb tremor and rigidity, one side often being affected more than the other. In this group there was evidence of minor, more widespread effects of the disease, such as excessive salivation, loss of voice volume, etc. The third group was made up of 17 patients with severe bilateral tremor and rigidity, tremor predominating. There were also marked widespread effects of the disease, including degrees of mental deterioration in some patients. These widespread effects suggested to us a more diffuse underlying pathology, and that these patients would tolerate operative lesions less well, producing more complications and side-effects, particularly when large lesions were made, and this has been largely confirmed. The aetiology in each case was mostly unknown. A few patients had a definite history of

TABLE I.—*Detailed Analysis of the Results of Surgical Treatment in 60 Patients with Parkinsonism*

Case No.	Sex and Age	Duration of Symptoms (Years)	Month and Year of First Operation	Side and Site of Lesions*	Effect of First and Subsequent Lesions								Widespread Manifestations of Parkinsonism (Excluding Limbs)						Post-operative Neurological Deficits	Result of Operations§ (Neurosurgeon, Neurologist, Psychologist)	Practical Success of Operations‖		Comments
					Limbs Contralateral to First Lesion				Limbs Ipsilateral to First Lesion				Tremor‡		Rigidity‡		Mental Deterioration‡						
					Tremor†		Rigidity‡		Tremor†		Rigidity‡												
					Preop.	Now	Preop.	Now	Preop.	Now	Preop.	Now	Preop.	Now	Preop.	Now	Preop.	Now			Preop.	Now	
1	M 50	24	Mar. 55	RP	90	0	2	0	0	0	0	0	0	0	1	0	1	1		A	*c*	*a*	
2	M 53	12	Jan. 57	RP	75	0	2	0	25	10	1	1	0	0	1	0	0	0		A	*c*	*a*	
3	F 50	5	Mar. 57	RP/6/LP	75	5	2	0	25	10	2	1	1	0	2	1	1	1		C	*d*	*c*	
4	F 50	8	Oct. 57	LP/10/RP	100	0	2	0	75	15	2	1	0	0	1	0	0	1		B	*c*	*c*	
5	M 63	6	Nov. 57	LP/28/RP/RT	100	0	2	0	70	20	2	0	1	0–1	1	0–1	1	0		A	*c*	*a*	
6	F 60	10	Dec. 57	RP/10 RT	90	15	1	0	50	50	1	1	0	0	1	1	0	0		A	*c*	*b*	
7	M 38	24	Jan. 58	LP/17/RTP	25	0	2	0	75	0	2	0	0	0	2	0	1	1	Dysphasia 6 weeks	C	*d*	*d*	Persisting festination
8	M 52	22	,, 58	LP	90	10	2	0	0	0	0	0	0	0	1	0	0	0		A	*b*	*a*	
9	M 54	5	Feb. 58	LP/9/LT	50	0	1	0	0	10	0	0	0	0	1	0	1	1		A	*d*	*c*	
10	M 53	6	Mar. 58	LP/¼/LP	75	0	2	0	50	20	2	1	2	1	2	1	1	0	,, 4 ,,	C→A	*d*	*b*	
11	M 54	6	,, 58	RP	100	0	3	1	70	90	2	2	1	1	2	1	0	0		B	*c*	*b*	,, ,,
12	M 47	13	,, 58	LP/14/RT	50	10	3	1	50	20	3	2	2	1	3	3	2	3		C	*d*	*e*	
13	M 57	9	Apr. 58	LP	75	20	2	1	40	30	2	1	0	0	2	1	1	1		B	*d*	*c*	
14	M 59	6	,, 58	LP/9/RT	80	50	2	1	40	20	2	1	2	1	1	1	1	1		B	*d*	*c*	Temporary deterioration during chronic urinary-tract infection. Improved again after prostatectomy. N.B. Festination
15	F 61	5	May 58	LP/15/RT	75	20	2	1	50	0	2	0	2	1	1	0	1	1		B	*d*	*b*	
16	M 62	10	,, 58	LP	10	0	3	1	5	5	3	2	0	0	3	1	2	1		B	*b*	*a*	
17	F 39	7	Jun. 58	RP/11/LT/2/RT	70	10	2	0	100	20	2	0	1	0	1	0	0	0		A	*c/b*	*b*	
18	F 57	11	,, 58	LP/6/LT	90	50	2	0	75	100	1	1	1	1	1	0	1	1		D	*c*		Fractured femur. Tremor returned. Suicide
19	F 51	23	,, 58	LP/7/RT/13/LT	90	10	2	0	50	0	2	1	1	0	2	1	0	0		B	*c*	*c*	Festination
20	M 51	5	,, 58	RP/5/RT	5	0	2	0	0	0	1	1	1	0	1	1	0	0		A	*b*	*a*	
21	M 39	4	,, 58	LP 27/RT/RP	5	0	2	0	10	10	1	1	0	0	1	0	0	0		A	*b*	*a*	
22	F 56	3	,, 58	LP/12/LT	75	0	2	0	0	0	1	0	1	0	1	0	0	0		A	*c*	*a*	
23	F 56	11	,, 58	RP/13/LT/LP	100	0	2	0	100	20	1	0	1	0	1	0	1	1		A	*c*	*b*	
24	M 61	16	Jul. 58	LP/8/RT	100	30	3	1	50	0	2	0	2	1	3	1	0	0		B	*d*	*c*	Temporary deterioration from fractured spine
25	M 45	7	,, 58	RP	5	0	2	0	0	0	1	2	0	0	1	1	1	0–1		A	*b*	*a*	Requires op. in contralateral hemisphere
26	M 57	20	Aug. 58	LT	75	25	1	0	0	0	0	0	0	0	0	0	0	0		B	*b*	*a*	
27	M 53	9	Oct. 58	RT	50	10	1	0	10	10	1	1	0	0	1	1	1	1		A	*b*	*b*	
28	F 52	4	,, 58	RP/LP/LT	50	0	2	1	50	10	2	1	0	0	1	0	1	1		A	*d*	*c*	
29	F 42	14	,, 58	RT/15/LP/LT	50	0	2	1	20	0	1	0	2	0	2	1	2	2		A	*d*	*d*	
30	F 52	1	,, 58	LT	50	0	2	0	0	0	0	0	0	0	1	0	1	1		A	*c*	*b*	
31	M 51	7	Nov. 58	LT	100	20	1	0	100	100	1	1	0	0	1	0	1	2		B	*c*	*d*	
32	M 33	4	,, 58	RT	100	0	2	0	0	0	0	0	0	0	1	0	1	1		A	*d*	*c*	
33	M 57	7	,, 58	RT	100	20	2	0	0	30	0	1	0	1	1	1	1	1		B	*b*	*b→c*	Requires op. in contralateral hemisphere
34	M 51	2	,, 58	LT	100	10	1	0	10	10	0	0	0	0	1	0	1	2		C	*d*	*d*	Post-op. psychosis—settled
35	M 58	13	,, 58	LT	100	0	3	1	100	100	3	2	0	0	3	1	1	1		B	*d*	*c*	
36	M 57	6	Dec. 58	LP/¼/RP	60	10	3	0	40	10	3	0	2	1	3	2	1	1		A	*d*	*c*	Muscle limb pain relieved by op.
37	M 63	1	,, 58	LT	80	0	0	0	20	10	0	0	1	1	1	0	0	0		A	*c*	*b*	
38	F 50	10	,, 58	LT	75	20	2	0	40	40	0	0	2	0	0	0	1	1		B	*d*	*b*	
39	M 50	10	Jan. 59	LT	10	0	3	0	0	0	3	2	0	0	2	1	1	1		A	*d*	*b*	
40	M 52	20	,, 59	RT	70	10	3	1	60	60	3	3	3	2	3	3	1	2		C	*e*	*e*	Died of pneumonia 3 months post-op. Severe chest-wall rigidity
41	M 72	7	,, 59	LT	50	5	1	0	0	0	0	0	0	0	0	1	1	1		A	*c*	*c*	
42	M 59	8	Feb. 59	LP/LT	50	0	3	0	60	60	3	2	1	0	3	2	2	2		A	*d*	*c*	
43	F 63	7	,, 59	LP	70	20	2	0	25	25	2	2	0	0	2	1	1	1		A	*d*	*c*	
44	F 53	9	,, 59	LT	100	10	1	0	50	50	0	0	0	0	1	0	1	1		A	*d*	*b*	
45	M 52	5	,, 59	RT/RP	75	0	2	0	0	20	0	1	0	0	1	0	0	0		A	*b*	*a*	May require op. in contralateral hemisphere
46	F 61	2	,, 59	RT/RP	75	0	1	0	10	10	0	0	0	0	1	0	0	0	Paraesthesia thumb and index fingers treated side for 2 months	A	*c*	*b*	
47	F 51	2	,, 59	RP	10	0	1	0	0	0	0	0	0	0	1	0	1	1		A	*b*	*c*	

TABLE I (*continued*)

TABLE I (*continued*)

Case No.	Sex and Age	Duration of Symptoms (Years)	Month and Year of First Operation	Side and Site of Lesions*	Effect of First and Subsequent Lesions: Limbs Contralateral to First Lesion — Tremor† Preop.	Tremor† Now	Rigidity‡ Preop.	Rigidity‡ Now	Limbs Ipsilateral to First Lesion — Tremor† Preop.	Tremor† Now	Rigidity‡ Preop.	Rigidity‡ Now	Widespread Manifestations of Parkinsonism (Excluding Limbs): Tremor‡ Preop.	Tremor‡ Now	Rigidity‡ Preop.	Rigidity‡ Now	Mental Deterioration Preop.	Mental Deterioration Now	Post-operative Neurological Deficits	Result of Operations§ (Neurosurgeon, Neurologist, Psychologist)	Practical Success of Operations‖ Preop.	Practical Success of Operations‖ Now	Comments
48	M 59	19	Mar. 59	LT LP	75	0	3	1	50	50	2	2	2	0	2	2	1	2		A	*d*	*d*	Added hypokinesis post-op.
49	F 43	20	,, 59	LT LP	90	0	3	0	75	50	3	2	1	0	2	1	1	0		A	*d*	*b*	
50	F 61	8	,, 59	LT LP/10/RT/RP	100	10	2	0	45	0	1	1	0	0	1	0	2	2		A	*b*	*b*	
51	M 55	6	,, 59	LT	50	10	2	0	10	10	1	1	0	0	1	0	2	2		C	*d*	*d*	Intermittent confusion pre-op. Tendency accentuated by op. Now improving
52	M 52	25	,, 59	RT RP	90	0	2	0	0	0	0	0	2	0	2	1	1	0		A	*d*	*b*	
53	F 64	1	,, 59	RT RP	100	0	1	0	75	80	1	1	0	0	1	0	1	1		A	*d*	*c*	
54	M 63	16	Apr. 59	LT LP	50	0	3	0	25	25	1	1	0	0	2	1	2	3		A	*d*	*b*	
55	M 58	10	,, 59	RT/RP	20	0	2	0	25	0	1	1	0	0	1	0	2	2		C	*d*	*c*	
56	M 60	10	May 59	RT/RP	20	0	1	0	0	0	1	1	0	0	2	1	2	3		A	*c*	*b*	Pre-op. increasing mental deterioration. Continuing to progress
57	M 51	7	,, 59	LT/LP	25	0	2	0	0	0	0	0	0	0	2	0	1	1		A	*b*	*a*	
58	F 38	2	,, 59	LT/LP	90	0	1	0	0	0	1	0	0	0	1	0	1	1		A	*d*	*b*	
59	F 62	8	,, 59	LT/LP	50	0	2	0	0	0	1	1	0	0	1	0	1	1	Temporary ataxia after operation	A	*c*	*b*	
60	M 57	3	,, 59	RT/RP	15	0	2	0	0	0	0	0	0	0	0	0	0	0		A	*b*	*a*	

* R=right; L=left; P=pallidum; T=thalamus. Intervals between operations stated in months. † Recorded as percentage depending on its duration each day. ‡ Graded on scale 0=nil; 1=minor; 2=moderate; 3=severe. § Result of operations in treated limbs in regard to rigidity and tremor. A=abolished; B=satisfactorily reduced; C=as A or B but with complications; D=unchanged or worse. ‖ Practical estimation of pre- and post-operative level of activities (patient, relatives, general practitioner). *a*=full working capacity; *b*=reduced working capacity; *c*=protected circumstances—minor home responsibilities; *d*=ambulant but requiring some nursing care; *e*=bedridden invalid requiring constant nursing care.

encephalitis, and in some in the older age-groups arteriosclerosis was the probable underlying pathology. We have deliberately used the term Parkinsonism somewhat loosely on this account.

TABLE II.—*Pre-operative Assessment of 60 Patients with Parkinsonism*

Tremor and Rigidity			Clinical Features Indicating Widespread Effects	
Unilateral	Bilateral		Tremor	Rigidity
Confined to limbs 19	Essentially confined to limbs; minor widespread effects 24	Marked widespread effects 17	Jaw Tongue Head	Face Voice Swallowing Salivation Trunk Thorax
			Mental deterioration	

TABLE III.—*Results of Surgical Treatment in Relation to Pre-operative Assessment (60 Patients)*

Results		Pre-operative Tremor and Rigidity		
			Bilateral Limbs	
Post-operative State of Tremor and Rigidity in Treated Limbs	No. of Patients	Unilateral Limbs (19 Cases)	Minor Widespread Effects (24 Cases)	Marked Widespread Effects (17 Cases)
Abolished ..	40	17	15 (5)	8 (3)
Significantly reduced ..	13	1	7 (2)	5 (4)
Abolished or reduced plus complications ..	6	1	2 (1)	3 (1)
Unchanged or worse ..	1	0	0	1
Death from operation	0	0	0	0

Figures in parentheses indicate bilateral operation.

In Table III the results of operative treatment are shown in relation to the three pre-operative groups of Table II. In 53 of the 60 patients limb tremor and rigidity were abolished or significantly reduced to give practical benefit. There were no complications in this group. Of the 60 patients, 16 had bilateral operations.

Complications

Six patients in Table III, despite successful treatment of limb rigidity and tremor, showed various types of complications. In two (Table I, Cases 7 and 10) moderately severe dysphasia followed operation in the dominant hemisphere, lasting four weeks in one and six weeks in the other. In both this was the result of misplaced lesions during the early development of the stereotaxic procedure. Subsequent charting showed the lesions to lie well within the internal capsule. Nevertheless, follow-up has shown an excellent over-all result in one and a fair result in the other, the latter due to persistence of festination and some degree of inertia. In both the dysphasia cleared up.

The third patient (Table I, Case 51), who had shown marked confusion before operation, developed a florid psychotic reaction as the electrode entered the thalamus of the dominant hemisphere. Consequently a smaller lesion than usual was made, but tremor and rigidity in the right limbs, and his general condition, showed definite improvement. The psychotic condition persisted for three weeks, but the fluctuating confusion present before operation persists. In this case the lesion was accurately sited.

The fourth patient (Table I, Case 34) was somewhat similar, for he developed a severe confusional state following operation on the thalamus of the dominant hemisphere. This also persisted for about four weeks, settling down to a somewhat fluctuating degree of confusion, which was largely part of the clinical picture

seen pre-operatively. Once more tremor and rigidity were largely relieved in the contralateral limbs. The lesion was again correctly sited.

The fifth patient (Table I, Case 3), following bilateral lesions in the globus pallidus with an interval of some eight months between each, shows a persistence of physical and mental inertia, though over-all improvement in this respect continues. This patient, early in the series, received a larger lesion than is now our practice. The second, and much smaller, lesion in the contralateral hemisphere was followed by this definite personality change.

The sixth and last patient (Table I, Case 12) to show complications was grossly disabled by his disease, and had been confined to a chair for some six years. After operation on the globus pallidus he was in a state of stupor for a few weeks, but gradually improved. The lesion was ill sited, being too anterior and too low, and in the neighbourhood of the striate vessels. The benefits ultimately obtained were sufficient to warrant consideration of the creation of a lesion on the other side. This was carried out some nine months after the first. It was unfortunately complicated by a haemorrhage into the left lateral ventricle. Thereafter he was comatose, and after many months of stupor he succumbed to a staphylococcal pneumonia.

Deaths

There were no immediate deaths from operation, but three patients have died since operation—one, the patient already described, from a ventricular haemorrhage, and the other (Table I, Case 40) from a staphylococcal pneumonia three months after operation. It was felt that, though the lesion in this second case was satisfactorily sited, it was too small, and a more radical lesion might have achieved a better result. A staphylococcal pneumonia complicated his convalescence from operation, and rigidity of his thorax, which had not been adequately relieved, made him a poor subject to withstand it. One other patient subsequently committed suicide after sustaining a fracture of the femur (Table I, Case 18). Recurrence of tremor had occurred following a fall and fracture of the femur. Thereafter she developed an acute depression and unfortunately died from coal-gas poisoning. She is included in Table III as "unchanged or worse."

Psychometry

Psychometric studies were carried out in the patients of the series both pre-operatively and at various stages post-operatively. The findings enabled us to estimate the degree of any pre-existing mental deterioration attributable to the disease in relation to such changes after operation, and are incorporated in Table I. Methods of assessment included the standard tests, Mill Hill Vocabulary Scale, Progressive Matrices (1938 version), Graham and Kendall Design Memory Test, and Rorschach Projection Test.

Evolution of Surgical Treatment

In achieving the results already described we have passed through three phases in the siting of the surgical lesions as experience accumulated. Table IV explains these phases. The first was from March, 1955, to July, 1958 (Table I, Cases 1–25), and lesions were made in the globus pallidus 17 mm. from the mid-line. In some of this group in whom tremor predominated the best

TABLE IV.—*Evolution of Surgical Treatment in 60 Cases of Parkinsonism*

Operation Dates	First Lesions		Further Lesions	
	Site	No. of Patients	Site	No. of Patients
March, 1955, to July, 1958	Pallidum	25	Ipsilateral pallidum	1
			,, thalamus	7
			Contralateral pallidum ..	2
			Contralateral thalamus ..	6
			Contralateral thalamus/pallidum	2
August, 1958, to January, 1959	Thalamus ..	14	Contralateral pallidum ..	1
	Pallidum	2	Contralateral .. thalamus/pallidum	2
February to June, 1959	Pallidum	2	Contralateral thalamus/pallidum ..	1
	Thalamus ..	2		
	Thalamus/pallidum	15		

results—that is, the elimination of tremor as well as rigidity—followed a lesion in the globus pallidus and ansa lenticularis or in the globus pallidus and adjacent internal capsule, or a lesion which included all these sites. When rigidity predominated, a lesion in the globus pallidus, between its medial and lateral parts, almost invariably gave good results. The failure to abolish tremor completely or the recurrence of rest tremor after some weeks led us to adopt the suggestion of Hassler (1957) that a lesion in the ventro-lateral nucleus of the thalamus might abolish tremor more effectively. Of 25 patients originally treated by lesions in the globus pallidus, 7 had an additional lesion made in the ipsilateral thalamus with abolition of persistent rest tremor. As a result, in Phase II, 14 patients from August, 1958, to January, 1959, were treated by thalamic lesions only, these being made in the ventro-lateral nucleus adjacent to the capsule, 16 mm. from the mid-line. Tremor was successfully abolished or greatly reduced in many more patients than previously, but rigidity did not resolve as completely as with lesions in the globus pallidus. As a result, in the last phase, from February to June, 1959, double lesions on the same side—one in the thalamus and one in the globus pallidus, both adjacent to the internal capsule—were made, with further improvement of results and without increasing morbidity. By lowering the trajectory of the track of the electrode 2 to 3 cm. below that advocated by Guiot (1958) both lesions could be made with the same track (Special Plate, Fig. 3, and text figure). In May, 1959, experience suggested the possibilities of a different type of lesion. Tremor in one patient was difficult to eliminate (Table I, Case 52), but by adjusting the position of the electrode in the sagittal plane several times, using low-coagulation current, we abolished tremor without the appearance of side-effects. On charting the lesion we found that it was narrow and elongated, starting in the thalamus, almost completely traversing the capsule, and ending in the globus pallidus 16 mm. from the mid-line and parallel to it. There were no neurological deficits. Tremor and rigidity in the contralateral limbs were abolished and facility was restored. Surprisingly perhaps, yet a matter of considerable importance, transient disturbance of consciousness, which had occurred many times a day for some years before operation and which grossly interfered with the patient's contact with others, disappeared and has remained absent for 15 months to date. This experience has led to further pursuit of this type of lesion in other more recent cases with

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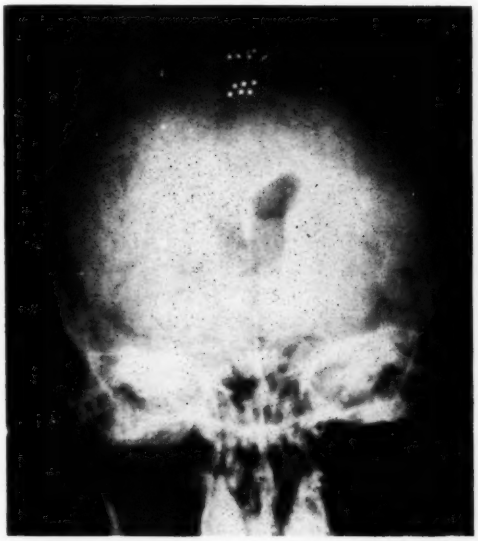

FIG. 1.—Postero-anterior air encephalogram showing radio-opaque markers in the frontal, coronal, and occipital regions which correspond to the mid-sagittal plane (septum pellucidum and third ventricle).

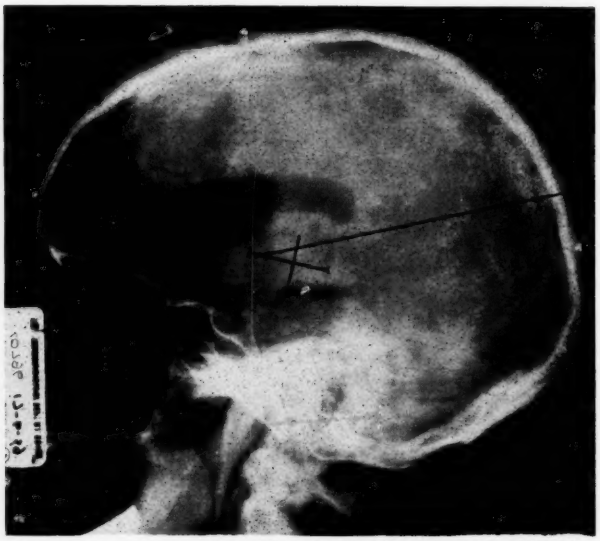

FIG. 3.—Determination of pallidal and thalamic target points and track of electrode from lateral air encephalograms superimposed to show the anterior and posterior commissures.

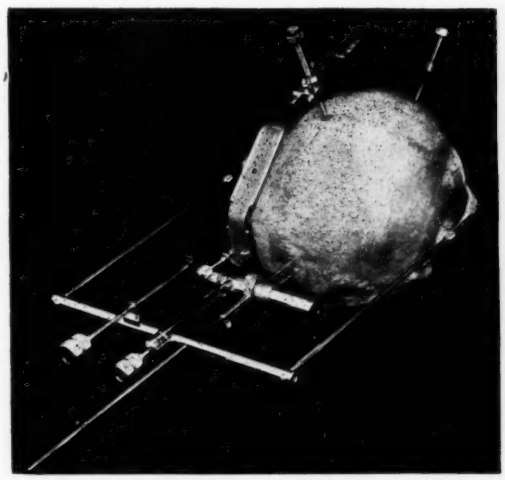

FIG. 2.—Stereotaxic apparatus applied to the skull.

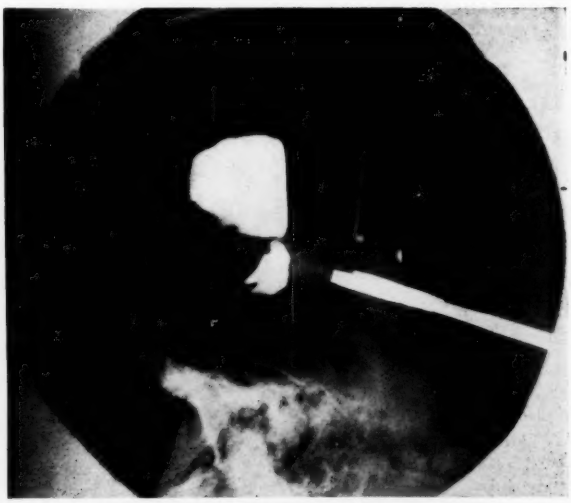

FIG. 4.—Sights aligned against pallidal target point.

Figs. 5 and 6 appear overleaf

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FIG. 5.—Brain of a patient, not of the present series, who died from coronary thrombosis eight weeks after operation. Sagittal section 17 mm. from the midline, showing lesions in the thalamus and globus pallidus.

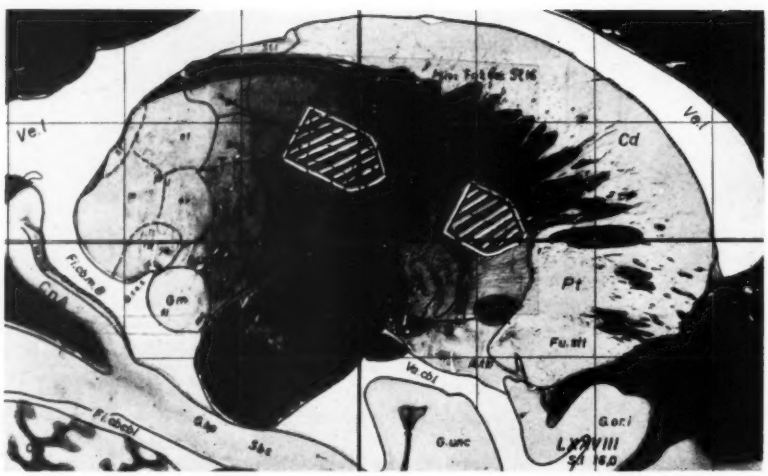

FIG. 6.—Lesions in the globus pallidus and thalamus plotted on a sagittal section (×3) 16 mm. from the midline. (Schaltenbrand and Bailey's (1959) atlas.)

G. B. LEITCH: AMYLOID TUMOUR OF LARYNX PRECEDING RHEUMATOID ARTHRITIS

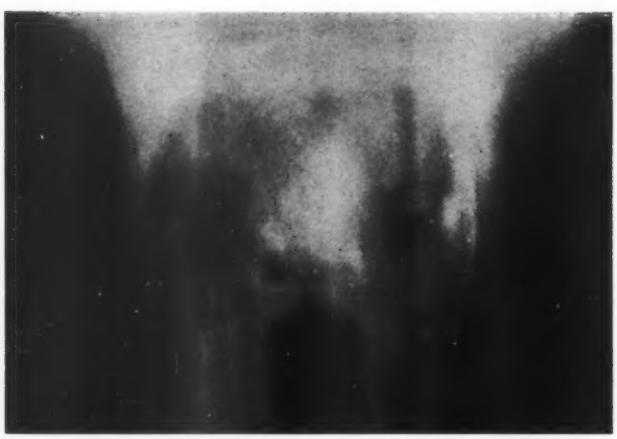

FIG. 1.—Tomograph of larynx (April 23, 1956) showing mass arising above glottis on left side and approximately central in position with some secondary dislocation of aryepiglottic fold on left side. Appearances favour a tumour arising from neighbourhood of false cords.

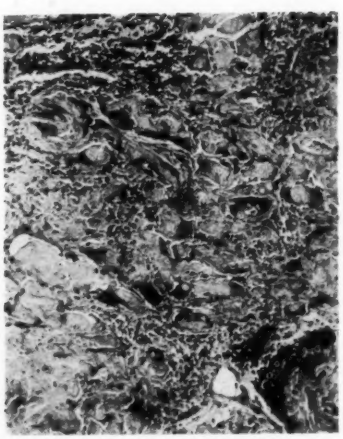

FIG. 2.—Section (April 25, 1956) showing amyloid occurring in small masses separated by fibroblasts and chronic inflammatory cells. Prominent giant-cell reaction is present.

bilateral Parkinsonism. They were successfully relieved, but one has the complication of minor paraesthesiae affecting the angle of the mouth and the tips of the thumb and index finger of the opposite limb. From these studies it would seem that tremor and rigidity are controlled most effectively by the strategic interruption of the thalamo-pallidal connexions, essentially the ansa and fasciculus lenticularis. Whether this can be best achieved in the capsule by a relatively small lesion or in the adjacent thalamus and globus pallidus is not yet clear. Certainly large lesions of the capsule in this area are followed by major deficits of motor, sensory, and language function, the last if the lesion lies in the dominant hemisphere. Fortunately we have been able, in the main, to avoid such lesions.

Discussion

A study of the results indicates the need for selection of patients for surgical treatment, and helps to define the pertinent features in the clinical picture which guide selection. The only absolute contraindication to operation is the definite evidence of increasing mental confusion of a moderately severe degree, not dependent on toxic reaction to drugs. Very advanced Parkinsonism—that is, chair- or bed-ridden patients—is not easily benefited by surgery, but some patients have responded dramatically, even to the extent of correction of a gross kyphosis. When the disease is rapidly advancing the duration of benefit is limited, and the converse applies when the disease appears to have halted or is only slowly progressive. In this respect it is important to recognize that we are, in the main, dealing with a progressive disease. However, it may be that strategically placed lesions of adequate size might halt the disease process. This is not yet clear.

Patients over 65 should be considered for surgery only when the disease is essentially unilateral and when they are in good physical and mental condition. Without question the best results are achieved in those patients under 60 in whom rigidity predominates and the disease is slowly progressive and only moderately advanced. Benefit from operative treatment may be lost temporarily during a period of intercurrent infection or emotional stress, or following an injury such as fracture of the femur.

The best type of lesion for the effective and prolonged relief of tremor and rigidity in this series would seem to be the double one, made at the same time in the ventro-lateral nucleus of the thalamus and in the globus pallidus 16 mm. from the mid-line, both lesions bordering on the internal capsule. Hemiparesis or disturbance of sensation are avoided if the lesions are not large and are confined mainly to the ganglia. Still under review is the effectiveness of long, thin lesions extending through the medial part of the posterior limb of the internal capsule from thalamus to pallidum. Early results of this lesion are encouraging. This particular method of stereotaxic cerebral surgery has the great merit of lending itself to the creation of lesions in the thalamus, internal capsule, or globus pallidus, using only one electrode track.

An explanation of the effectiveness of these lesions is not easy, but it may well be that they interrupt the pallidothalamic connexions; usually the ansa lenticularis and the fasciculus lenticularis, and possibly, in addition, connexions of these ganglia with the reticular formation.

Bilateral lesions in the treatment of bilateral Parkinsonism, provided they are small and strategically placed, would seem to be eminently practicable. Morbidity is so small as to recommend such a procedure, but usually with an interval of three to six months between the two operations. Two patients had lesions made bilaterally in rapid succession, one after minutes and the other after ten days (Table I, cases 28 and 36). The first showed some minor disturbance of recent memory which improved slowly, but there was a dramatic relief of Parkinsonism. The second showed no disturbance from bilateral pallidal lesions, the two operations following each other after ten days because of severe intractable pain from rigidity. Pain and rigidity were completely relieved and a severe kyphosis was largely corrected. A number of patients with Parkinsonism complain of pain in rigid limbs, often diagnosed as sacro-iliac pain, sciatica, rheumatism, or fibrositis. In some it is a predominant symptom. Rigidity also manifests itself in difficulty in turning over in bed, in getting out of a chair, and in swallowing. All these symptoms are markedly relieved.

Other associated symptoms which may disappear after operation are the minor attacks of disturbed consciousness and loss of concentration. Both can be benefited. Patients often report a return of their sense of well-being, and put on weight previously lost.

Post-operatively (even after unilateral operation in bilateral disease) drugs can be reduced to approximately half the original dosage, and sometimes given up altogether. This not infrequently results in some feeling of improvement in intellectual performance and sense of well-being from reduction of toxicity from the drugs.

One patient of considerable interest had moderately severe diabetes mellitus associated with Parkinsonism, and required heavy insulin dosage and a carefully supervised diet. After operation both conditions were relieved, the dosage of insulin being reduced to less than half its pre-operative level. Whether the operation had a specific effect on the diabetic condition at a hypothalamic level or whether there is some other explanation is not yet clear. Certainly in patients with Parkinsonism in whom rigidity is marked, loss of weight is a characteristic feature.

When discussing the question of surgical treatment with patients and their relatives it is important that they should know what can or cannot be achieved, and the possible hazards. The features of the disease which are benefited and the duration of relief have already been outlined. We have found that some symptoms are poorly relieved, if at all, and our experience coincides with that of others (Cooper, 1955). The festinant gait, oculogyric crises, reduction of voice volume, and excessive salivation remain difficult problems; indeed, the first two are seldom helped to any extent. Reduction of voice volume has been relieved in a few patients by about 10%, but the results in this respect are disappointing. Excessive salivation is dependent on excessive production, difficulty in swallowing, and to some extent on gravity—that is, in those with a marked kyphosis. Operative treatment helps to some extent only, by restoring swallowing and correcting the kyphosis by reduction of rigidity. In the intractable cases we have found that repeated small doses of radiotherapy to the salivary glands are of definite value.

Summary

An unselected series of 60 patients with Parkinsonism have been treated by stereotaxic electrocoagulation cerebral lesions. Of these patients 53, or 88%, have had tremor and/or rigidity abolished or significantly reduced without complications in the treated limbs, and have been followed for up to five years. Six patients, despite successful treatment of limb tremor and/or rigidity, have persisting complications of the operations. In only one case have limb tremor and rigidity been unimproved. These results have been achieved by accurate siting of the lesion and by making it as small as would be compatible with maintained improvement. The method used has evolved progressively, and is unique in allowing the creation of lesions in the globus pallidus, internal capsule, or thalamus with one electrode track at different depths. Such combined lesions are usually necessary to eliminate contralateral limb rigidity and tremor.

As a result of our experience we believe that the selection of patients for operation should be governed by the degree of widespread manifestations of Parkinsonism pre-operatively. Where widespread manifestations are present, surgical lesions to treat limb tremor and rigidity cannot be large or inexactly placed, otherwise mental deterioration characterized particularly by akinesis will be accentuated.

We wish to thank Professor Norman M. Dott for his interest in this research project; also those of the staff of the Department of Surgical Neurology who have assisted in this work, in particular Dr. A. F. J. Maloney, neuropathologist, and those who assisted in the anatomical charting of the lesions—Dr. Y. Peng Huang, Dr. B. Sira, and Dr. A. Caracalos. Mr. George Newell, of the Department of Animal Genetics of the University of Edinburgh, was initially responsible for the manufacture of the instrument, and has greatly assisted in its elaboration.

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Of the six countries which have the lowest infant mortality in the world, four are European. Statistics for 1958 published by the World Health Organization give the following infant mortality figures per 1,000 live births: Sweden, 16; the Netherlands and Iceland, 17; New Zealand, 19; Australia, 20; Switzerland, 22.

DIGITALIS AS A CAUSE OF PAROXYSMAL ATRIAL TACHYCARDIA WITH ATRIOVENTRICULAR BLOCK

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Digitalis remains probably the most useful single drug in the treatment of all forms of heart failure, though its injudicious use may result in a wide variety of toxic effects on the myocardium. Almost every form of arrhythmia and conduction defect has been attributed to the toxic effects of the drug, most of them arising from the action of digitalis on the ventricles.

The purpose of this paper is to draw attention to an important effect of over-digitalization on the atria—namely, paroxysmal atrial tachycardia with atrioventricular block (P.A.T.B). The frequency and gravity of this form of digitalis intoxication does not seem to be widely appreciated, yet in certain circumstances very little digitalis can prove fatal. The frequency with which this arrhythmia may result from digitalis is well recognized in the American literature, owing to the work of Lown and Levine (1958), who have summarized their experience in book form. However, it appears to have escaped emphasis in this country, and it does not receive mention in the standard textbooks, where paroxysmal atrial tachycardia is usually dismissed as being of little clinical consequence. This is all the more surprising because it was, in fact, Lewis in 1909 who first described the arrhythmia, and Mackenzie (1911) who attributed it to digitalis.

There is no doubt that digitalis poisoning is occurring with increased frequency, and this is almost certainly due to the greater part played nowadays by therapy which affects the blood electrolytes, particularly the potassium. Among such therapeutic measures may be mentioned the use of salt-reduced diets, potent diuretics both mercurial and of the chlorothiazide type, ammonium chloride, especially if used continuously, cation-exchange resins, and corticosteroids. The importance of the early recognition of this arrhythmia lies in the fact that if it is mistaken for atrial flutter or atrial fibrillation, digitalis may be given, or the dose increased, with fatal results. Similarly, if paroxysmal atrial tachycardia is present but digitalis is not recognized as the cause, the dose may be mistakenly increased, as it is usually regarded as the drug of choice in that condition. In fact, Friedberg (1956) recommends the intravenous route. Provided digitalis is recognized as the cause of the arrhythmia and appropriate treatment given, the prognosis is, in our experience, less serious than has been claimed, and 9 of our 11 patients survived.

Material and Methods

We present the findings in 11 patients, collected over the past two years, in whom P.A.T.B. was present and in all of whom digitalis was believed to have played a major part in precipitating the arrhythmia (Table I).

TABLE I.—*Factors Precipitating Paroxysmal Atrial Tachycardia with Atrioventricular Block*

Case No.	Age and Sex	Digitalis prior to P.A.T.B.	Other Causative Factors					Serum K (mEq/l.)	Blood Urea (mg./100 ml.)
			Diuretics	Salt Restriction	Steroids	Ischaemia	Others		
1	68 F	Digoxin 0·75 mg./day for 4 months; 1 mg./day for 6 days	Mersalyl	Yes	No	No	Uraemia	3·8	74
2	50 F	Digoxin 0·5 mg. I.M., 0·5 mg. I.V., and 1 mg. orally all during 24 hours	No	No	No	No	—	—	—
3	48 M	Digitalis folia 3 gr. (0·2 g.)/day for 1 year	Chlorothiazide. Mersalyl	Yes	No	No	—	—	—
4	49 F	Digoxin 1·5 mg./day for 2 months; 0·5 mg. day for 11 days	No	No	No	No	—	—	—
5	67 F	Digoxin 1 mg. 1st day; 0·75 mg./day for 5 days	Chlorothiazide	Yes	Dexamethasone	No	—	4·5	24
6	63 M	Digoxin 1 mg./day for 2 days	,,	Yes	Prednisone	No	Cholangitis. Uraemia	6·0	89
7	39 F	Digoxin 0·5 mg./day for 130 days	,,	Yes	No	No	Childbirth 1 day prior. Carbimazole	—	—
8	51 F	Digoxin 1·25 mg. I.V. over 24 hours	No	No	No	No	Small-bowel obstruction. Gastric aspiration. Intravenous therapy	3·7	44
9	56 M	Digoxin 0·5 mg./day for 30 days	Mersalyl. Acetazolamide. Thiomerin	Yes	No	L.B.B.B.	Renal failure	4·4	50
10	58 M	Digoxin 3·5 mg. over 24 hours	Chlorothiazide	Yes	No	No	—	3·9	41
11	67 F	Digitalis folia 1½ gr. (0·1 g.)/day for 24 days; digoxin 0·5 mg./day for 11 days	Chlorothiazide. Mersalyl	Yes	No	Old cardiac infarct	—	3·8	85

The criteria by which the importance of digitalis as a cause was assessed were as laid down by Lown *et al.* (1959). All but one of the patients had 12-lead electrocardiograms taken before, during, and after the arrhythmia. All were followed until the P.A.T.B. had ceased and had been replaced either by sinus rhythm or by atrial fibrillation. Ten of the patients had heart disease and seven were in congestive heart failure at the time of the arrhythmia (see Table II). In addition, we

TABLE II

Number of cases	11
Heart disease	10
Mitral stenosis	4*
Hypertensive heart disease	2
Chronic cor pulmonale	2
Ischaemic heart disease	2
No heart disease	1
Congestive heart failure	7

* One patient also had thyrotoxicosis.

investigated in some detail a patient suffering from P.A.T.B. and congestive heart failure to whom no digitalis had ever been given, and this is discussed later.

Case Histories

Case 1.—A woman of 68, who had hypertensive heart failure and atrial fibrillation, was treated by sodium restriction and 0.75 mg. of digoxin daily for four months, and after admission to hospital the dose was increased to 1 mg. daily. Mersalyl 2 ml. was given intramuscularly on two occasions and sodium restriction was maintained. No diuresis resulted. Renal function was impaired, as shown by a raised blood urea of 74 mg./100 ml. Six days after admission a regular tachycardia of 140 a minute was noted, and in addition she was nauseated and had xanthopsia. An electrocardiogram showed an atrial tachycardia of 150 a minute with 2:1 block and digitalis effect on the RS–T segment and T wave. The serum potassium at that time was 3.8 mEq/l. Digoxin was stopped and no other therapeutic measures were taken. Within two days atrial fibrillation returned. When seen two years later she was clinically well but the atrial fibrillation persisted.

Case 2.—This patient was a woman of 50 with mitral stenosis and atrial fibrillation. Following on an embolus to the left leg her ventricular rate rose to about 300 a minute. In an effort to control this 2 mg. of digoxin was given over a period of 24 hours, part intravenously, part intramuscularly, and the rest by mouth. In spite of this the ventricular rate did not fall and a further electrocardiogram revealed paroxysmal atrial tachycardia with a 2:1 block and ventricular extrasystoles and S–T segment depression due to digitalis. During the atrial arrhythmia a pulmonary infarct occurred, followed by absorption collapse of the left lung. Digoxin was stopped and quinidine was given by mouth. After 106 gr. (7 g.) had been given over four days sinus rhythm was established. Six months later mitral valvotomy was performed, and she was well and in sinus rhythm 11 months afterwards.

Case 3.—A man aged 48 with congestive heart failure secondary to bronchitis and emphysema had been treated for one year with digitalis folia 3 gr. (0.2 g.) daily, mersalyl 2 ml. twice weekly intramuscularly, and sodium restriction. Because of an increase in his heart failure he was admitted to hospital, and to the above treatment was added chlorothiazide 1 g. daily for four days a week. Paroxysmal atrial tachycardia with a variable 2:1 and 3:1 block resulted. This responded when digitalis was stopped, the sinus rhythm then returning. He was well nine months later.

Case 4.—A woman of 49 with mitral stenosis and atrial fibrillation was admitted to hospital for consideration of mitral valvotomy. Digoxin 1.5 mg. daily had been given for the preceding two months, but this was reduced to 0.5 mg. a day on admission. After 11 days paroxysmal atrial tachycardia with variable 2:1 and 3:1 block developed. The electrocardiogram also showed ventricular extrasystoles and digitalis effect. On stopping digoxin and giving potassium chloride 3 g. daily, atrial fibrillation returned. Four days later mitral valvotomy was performed, but she died the same day. At necropsy a technically successful mitral valvotomy was found and there was no obvious cause for her sudden death.

Case 5.—A woman of 67 with mitral stenosis, but still in sinus rhythm, also had severe eczema and a hiatus hernia. She developed congestive heart failure as a result of atrial fibrillation with a rapid ventricular rate. Her sodium intake was therefore restricted and 4.75 mg. of digoxin was given over six days together with chlorothiazide 2 g. daily for four days a week. Dexamethasone 1 mg. daily was given because of the severity of her skin condition. Six days after starting digoxin paroxysmal atrial tachycardia with a variable 2:1 block developed. The level of the serum potassium was normal (4.5 mEq/l.) at this point. as was her blood urea (24 mg./100 ml.). Digoxin was stopped and she was given potassium chloride 5 g. daily for two days, at the end of which time sinus rhythm returned. She was alive and well two months later.

Case 6.—A man aged 63 was admitted to hospital with hypertensive heart failure and in sinus rhythm. In the past he had had a pyrexia of unknown origin thought to be due to a systemic collagen disease, and was treated for 18 months with prednisone 12 mg. daily. Over a period of two days 2 mg. of digoxin and 3 g. of chlorothiazide were given and sodium restriction was maintained. Paroxysmal atrial tachycardia with a 2:1 block developed within two days of starting digoxin. The serum potassium level at this point

was 6 mEq/l., while the blood urea was elevated to 89 mg./100 ml. Digoxin was discontinued, and after two days sinus rhythm returned. One month later he was alive and well.

Case 7.—A woman of 39, 32 weeks pregnant, was in sinus rhythm with mitral stenosis and thyrotoxicosis. The thyrotoxicosis was treated with carbimazole 20 mg. daily. Because of a persistent sinus tachycardia and dyspnoea digoxin was used, 0.25 mg. b.d. for 130 days. In addition, for one month, she was given chlorothiazide 2 g. daily for four consecutive days, supplemented with potassium chloride 3 g. daily on the remaining three days of the week. Sodium restriction was also maintained. She had a normal delivery, but next day paroxysmal atrial tachycardia with 2:1 block developed. In order to restore sinus rhythm, which was achieved after 12 hours, it was necessary to stop the digoxin and chlorothiazide, increase the potassium chloride to 6 g. daily, and give quinidine to a total of 50 gr. (3.2 g.). Six months later a successful mitral valvotomy was performed, but the sinus rhythm was replaced by atrial fibrillation, which has since persisted.

Case 8.—A woman aged 51 was admitted to hospital with small-bowel obstruction and no previously known heart disease. Gastric suction and intravenous therapy resulted in hypokalaemia, and an atrial tachycardia without block developed. This was treated with digoxin, 1.25 mg. being given intravenously over 24 hours. Paroxysmal atrial tachycardia with block developed the next day and the serum potassium level was then 3.7 mEq/l. The electrocardiogram showed RS-T segment depression due to digitalis. Digoxin was discontinued and potassium was given slowly intravenously in a strength of 1 g. to the pint (570 ml.). Sinus rhythm returned within three days. When seen three months later she was well and the electrocardiogram was normal.

Case 9.—A man of 56 was admitted to hospital with congestive heart failure. He was in sinus rhythm with left bundle-branch block due to ischaemic heart disease. B.P. 180/120 mm. Hg. During his stay in hospital pulmonary infarction developed. For a month digoxin 0.5 mg. daily was used together with sodium restriction and diuretics. At first mersalyl 2 ml. twice weekly was given, then acetazolamide 250 mg. daily three days a week, and finally "thiomerin" 2 ml. twice weekly. Despite these measures congestive heart failure progressed and paroxysmal atrial tachycardia with a variable 2:1 block developed. The electrocardiogram also showed evidence of digitalis effect. The serum potassium level was normal (4.4 mEq/l.) but the blood urea was 50 mg./100 ml. The tachycardia was treated at first with procainamide 1 g. by mouth over a period of one day while digoxin was continued. On the next day, as no effect had been noted, procainamide was discontinued and the digoxin was increased to 1 mg. over 24 hours, still with no effect. His condition was desperate, and thereafter quinidine was given intravenously to a total of 36 gr. (2.3 g.), but he died the same day. Necropsy was not performed.

Case 10.—A man aged 58 was admitted to hospital in gross congestive heart failure due to cor pulmonale. He was in sinus rhythm. One year prior to this admission he had been admitted in congestive failure and responded to treatment with rest in bed, salt-restriction, and mersalyl injections 2 ml. intramuscularly twice weekly. Digitalis was not used. On his present admission 1.5 mg. of digoxin was given, followed by 1 mg. eight hours later and 0.5 mg. each eight hours thereafter. Chlorothiazide 1 g. was also given on admission and 1 g. b.d. next day. On the second day of his admission an electrocardiogram showed paroxysmal atrial tachycardia with regular 2:1 block, and carotid sinus compression produced a variable block. The serum potassium was 3.9 mEq/l. The arrhythmia was treated by discontinuing digoxin and chlorothiazide and giving potassium chloride by mouth to a total of 6 g. daily, and by the following day sinus rhythm was restored. One day thereafter a regular atrial tachycardia with 2:1 block developed. Digoxin was recommenced with 0.25 mg. t.d.s., and potassium was again given by mouth. Sinus rhythm returned within 24 hours and has remained.

Case 11.—A woman of 67 was admitted to hospital in congestive cardiac failure of six months' duration. In 1955 myxoedema was diagnosed, and since then she had taken 3 gr. (0.2 g.) of thyroid daily. Prior to admission, treatment for her heart failure consisted of digitalis folia 1½ gr. (0.1 g.) daily and chlorothiazide 1 g. with potassium chloride 2 g. for five consecutive days of each week. As no diuresis resulted chlorothiazide was replaced by mersalyl, but in spite of a good diuresis she remained oedematous. When admitted 0.25 mg. of digoxin b.d. and mersalyl 2 ml. intramuscularly on alternate days were given; her intake of fluid and salt were restricted. The serum electrolytes showed moderate reduction of the sodium and chloride with no potassium depletion. The blood urea was elevated to 69 mg./100 ml.; plasma cholesterol 75 mg./100 ml. The electrocardiogram showed sinus rhythm with right bundle-branch block and signs of an old transmural anteroseptal infarct. Ten days after admission she felt depressed and complained of nausea and loss of appetite. The pulse was rapid and irregular, and an electrocardiogram showed paroxysmal atrial tachycardia with block, multifocal ventricular extrasystoles, and S-T segment depression and T-wave change due to digitalis. The level of potassium had now fallen to 3.8 mEq/l.; the blood urea had risen to 85 mg./100 ml. Digoxin was discontinued and potassium chloride 3 g. daily was given by mouth. Three days later sinus rhythm returned and has remained.

Discussion

Until recently it was thought that one of the essential differences between paroxysmal atrial tachycardia and atrial flutter was that in the former the ventricles responded to every supraventricular impulse, whereas in the latter some degree of atrioventricular block, constant or variable, was present. Although a few electrocardiograms of P.A.T.B. had been published previously, it was not until 1943 that it was realized that this arrhythmia is by no means rare. In that year Barker *et al.* published details of 17 previously recorded cases and added 18 more of their own, and later Evans (1944) attempted to establish the identity of paroxysmal tachycardia and atrial flutter. In both paroxysmal atrial tachycardia and atrial flutter the ventricular rhythm may be regular or irregular, and the distinction that atrioventricular block is present only in flutter is no longer valid.

Other differences often quoted as evidence of the separate identity of the two arrhythmias are, first, that carotid sinus compression and stimulation of vagal reflexes by other methods may abolish paroxysmal atrial tachycardia but does not have this effect on atrial flutter; secondly, in atrial tachycardia the atrial rate is said rarely to exceed 200 a minute and is often slower, whereas in flutter the atrial rate is faster; finally, the administration of potassium in digitalis-induced P.A.T.B. will almost always stop the arrhythmia, whereas it is ineffectual in atrial flutter. However, it is usually admitted that at times even the electrocardiograph may fail to distinguish the two arrhythmias, and from our studies we are convinced that there is no single criterion, either clinical or electrocardiographic, by which these two arrhythmias can be rigidly separated. All grades exist between classic flutter with "saw teeth" f waves in every lead and classic P.A.T.B. with small upright P waves in the standard leads and separation of the P waves by an isoelectric baseline in all leads. We do not consider that P.A.T.B. is a separate and distinct entity. It often represents a transitional stage between sinus tachycardia and flutter.

Prinzmetal *et al.* (1952) have produced convincing experimental evidence that distinction between P.A.T.B. and flutter is unwarranted. It is not uncommon for an

electrocardiogram to show both flutter and P.A.T.B. (Fig. 1), and in one of our patients carotid sinus pressure changed P waves typical of P.A.T.B. to waves resembling those of flutter. This interchangeability of rhythm was well known to Lewis (1912). We feel that attempts to construct tables purporting to reveal differences of importance between P.A.T.B. and flutter are to a large extent artificial and arbitrary and serve no useful purpose. The only question of real importance when an electrocardiogram is suspected of revealing P.A.T.B. is whether the arrhythmia is due to digitalis, because if it is then the patient is dangerously near the lethal toxic dose. The differences between P.A.T.B. without digitalis and due to that drug are tabulated (Table III), but occasionally it is impossible to be certain on clinical or electrocardiographic grounds whether digitalis has been given, and it has been pointed out elsewhere that in such cases the telephone may prove a more important diagnostic instrument than the electrocardiograph.

TABLE III.—*Differential Diagnosis of Paroxysmal Atrial Tachycardia with Atrioventricular Block*

	Digitalis-induced	Not due to Digitalis
Carotid sinus pressure:		
Atrial rate	Unchanged (i.e., no decrease)	Decreased
Degree of A–V block	Increased	Increased
Effect on P.A.T.B.	Nil	May stop
Atropine:		
Atrial rate	Unchanged (i.e., no increase)	Increased
Degree of A–V block	Decreased	Decreased
Procainamide; quinidine ..	May be effective	Often effective
Cholinergic drugs	Rarely ,,	,, ,,
Potassium	Effective	No effect
Electrocardiogram	Ventricular extrasystoles often, occasionally multi-focal	Rare, not multifocal
	Sagging of S–T segment	Absent

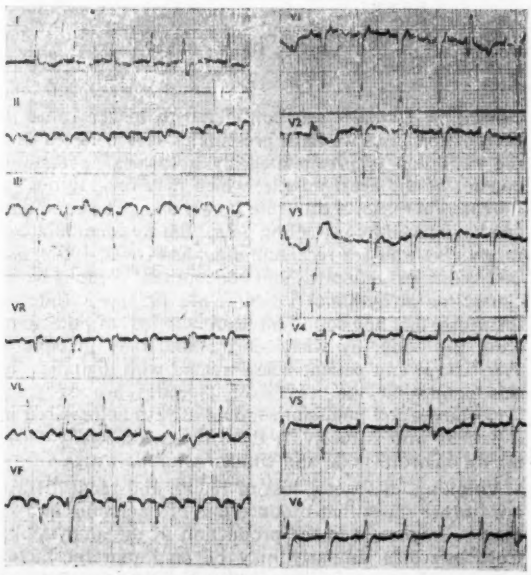

FIG. 1.—Leads II, III, and VF show atrial waves of "saw tooth" pattern resembling atrial flutter, yet the chest leads show diminutive, upright, pointed P waves characteristic of paroxysmal atrial tachycardia.

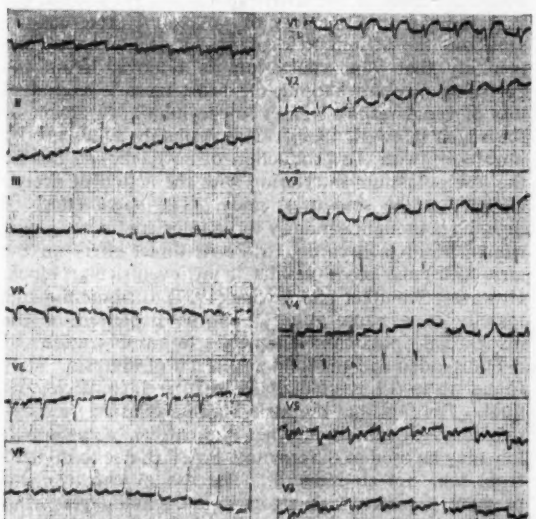

FIG. 2.—Paroxysmal atrial tachycardia with 2:1 block. The atrial rate is 376 a minute.

Characteristics of Blocked Paroxysmal Atrial Tachycardia

Lown and Levine (1958) have summarized these characteristics as follows:

1. An atrial rate of about 200 a minute. An arbitrary ceiling of 250 a minute has been set by these authors, but in some of their patients this was exceeded and the range was 100–270. In our series the atrial rate exceeded 250 in 3 out of 11 patients. In one patient (Case 7) it was 376 a minute (Fig. 2).

2. Change in contour of the P waves, which remain upright, though nearly always diminutive, in standard leads II and III.

3. An isoelectric baseline separates the P waves. This they regard as a *sine qua non*, and if even a single lead, extremity or precordial, showed continuous undulations of the baseline not attributable to T or U waves the patient was arbitrarily excluded as a probable case of atrial flutter. However, Kennamer and Prinzmetal (1954) have denied that the differentiation between flutter and P.A.T.B. may be made by the presence of an isoelectric interval between the P waves, and Simonson and Berman (1951) have stated that some patients may show isoelectric baselines in the chest leads and typical flutter waves in the limb leads (Fig. 1). Lown and Levine (1958) classified such patients as examples of atrial flutter. We consider that, although the most constant electrocardiographic characteristics of P.A.T.B. are the presence of an isoelectric interval between successive P waves and the absence of typical "saw teeth" f waves, occasionally the isoelectric segment may be absent. In some of our patients the atrial rate was so rapid that no intervening flat segment was present—for example, Case 7 (Fig. 2)—yet the P waves were diminutive and not of the typical form seen in flutter.

4. A variable degree of atrioventricular block. This is, of course, present by definition. Although paroxysmal atrial tachycardia without block may result from digitalis it is invariably short-lived and block soon appears.

5. Vagal stimulation, such as carotid sinus pressure, tends to augment the atrioventricular block but does not usually influence the atrial rate (Figs. 3 and 4).

The P wave may be so small that it is barely visible at times, and special leads may be required to reveal any atrial deflection. Evans (1944) favours lead CR1; at times lead V3R unmasks the P wave, but occasionally an oesophageal or deep epigastric lead is necessary. The P waves differ in contour from patients in sinus rhythm. In the series of Lown and Levine (1958) the mean atrial rate was 182, the range being 150 to 200, and in 76% of episodes the atrial rate was less than 200. The atrial rate in our series varied from 120 to 376. Unlike in flutter or classical atrial tachycardia, the P–P

interval in successive cycles may vary in duration, and at times this can be appreciated without measurement (Fig. 5 A). The degree of block varies from a 1:1 response with an occasional blocked beat associated the Wenckebach phenomenon to complete atrioventricular block, but the atrioventricular response is usually less than 2:1.

Evidence of digitalis intoxication was present in 73% of their cases and one-half showed ventricular premature beats. In contrast, all of our 11 patients showed the effect of digitalis on the electrocardiogram, whereas the incidence of ventricular premature beats was similar to that in their series—namely, 6 out of 11 (Table IV).

Digitalis is undoubtedly the most important single factor in the production of this arrhythmia, and in the series recorded by Lown (1957) 75% of episodes of P.A.T.B. were the result of digitalis intoxication. We wish to draw attention to the fact that the dose of digitalis does not have to be excessive, and it need not be accompanied by other signs of digitalis intoxication

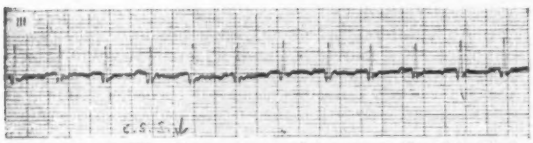

FIG. 3.—Lead III. Paroxysmal atrial tachycardia with block. Carotid sinus compression does not cause slowing of the atrial rate.

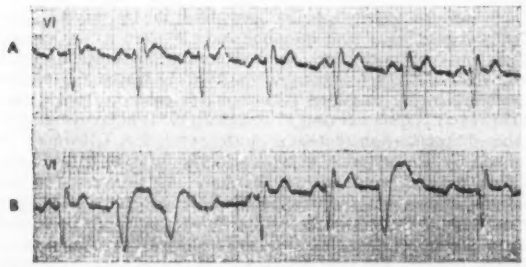

FIG. 4.—A, Lead V1. Paroxysmal atrial tachycardia with 2:1 block. Atrial rate 214 a minute. B, Lead V1. On compression of the left carotid sinus the atrial rate remains unaltered but the degree of block increases. Ventricular extrasystoles are present.

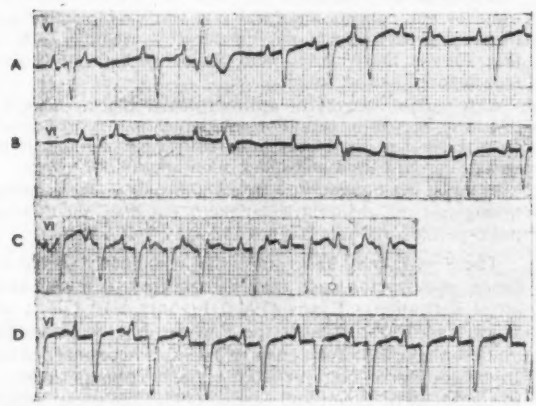

FIG. 5.—A, Lead V1. Paroxysmal atrial tachycardia with block. Atrial rate about 150 per minute. No digitalis had been given. B, Lead V1. On carotid sinus compression atrial rate now 100 per minute C, Lead V1. Three minutes after 0.65 mg. atropine intravenously atrial rate 250 per minute. D, Lead V1. After 400 mg. procainamide intravenously regular sinus rhythm.

TABLE IV.—*Analysis of Electrocardiographic Findings*

Case No.	Signs of Dig. Toxicity	Original Rhythm	P.A.T.B. Duration	P.A.T.B. Atrial Rate	P.A.T.B. A–V Block	P.A.T.B. Ventric. Extrasyst.	Final Rhythm
1	Yes	A. Fib.	2 days	275	2:1	Absent	A. Fib.
2	,,	,,	2 ,,	300	2:1	Present	Sinus, reverted to P.A.T.B., finally sinus
3	,,	Sinus	1 day	250	2:1 and 3:1	Absent	Sinus
4	,,	A. Fib.	1 ,,	214	2:1 and 3:1	Present	A. Fib. Died
5	,,	Sinus	2 days	180	Variable 2:1	Absent	Sinus
6	,,	,,	2 ,,	150	2:1	,,	,,
7	,,	,,	12 hours	376	2:1	Present	,,
8	,,	—	2 days	120–150	2:1	Absent	,,
9	,,	Sinus L.B.B.B.	2 ,,	188	Variable 2:1	Present	P.A.T.B. Died
10	,,	Sinus	1 day	214	Variable 2:1	,,	Sinus
11	,,	,,	3 days	115	Variable	,,	,,

clinically. Digitalis was considered to be the cause in each of the cases we have presented. It is believed that the condition is precipitated by a lowered potassium content of the heart muscle, which may or may not be mirrored in the level of serum potassium. The condition can be induced by extracting potassium by haemodialysis in patients who are receiving digitalis (Lown, 1957), but potassium loss alone without concomitant digitalis never causes the arrhythmia (Lown *et al.*, 1953). It follows, therefore, that any condition leading to loss of potassium from the body, by whatever method, may precipitate P.A.T.B. in any patient being treated with digitalis. In this connexion the effects of diuretics are of great importance, and potassium should always be replaced in a patient who is receiving these drugs, especially those taking chlorothiazide and similar saluretic drugs.

Vomiting, diarrhoea, loss of blood, and renal disease are further states that produce loss of potassium and so may be important in the production of the arrhythmia. Corticosteroids similarly may be an important factor when used in conjunction with digitalis, and were a precipitating cause in two of our patients (Table I).

The exact mechanism by which the loss of myocardial potassium leads to the arrhythmia is not yet known, but it is thought that the loss of potassium preferentially sensitizes the atrium to digitalis. It is known experimentally that when potassium is removed from the perfusing medium bathing the heart there is a gradual loss of atrial responsiveness to the inhibitory action of the vagus (Howell, 1906). This probably arises not by interfering with the production of acetylcholine but by the low potassium interfering with the action of acetylcholine on the sino-atrial node. The vagal effect of digitalis is thought similarly to be interfered with, giving rise to atrial tachycardia, while its direct effect on the atrioventricular node results in atrioventricular block. However, Schnitker and Levine (1937) attribute digitalis toxicity to a cause other than the depletion of the myocardial potassium—namely, to mobilization of digitalis-laden oedema fluid as a result of diuresis. They found up to 0.1 g. of digitalis leaf per litre of oedema fluid. The fact that the atria become relatively insensitive to vagal inhibition when the cardiac potassium is low may be used to differentiate P.A.T.B. due to digitalis from that not so induced. The use of carotid sinus pressure together with atropine and cholinergic drugs such as neostigmine and mecholyl for this purpose is described later (and see Table III).

The frequency of congestive heart failure in patients with P.A.T.B. due to digitalis has been emphasized by Lown (1957), all but 6 of his 64 patients being in congestive heart failure at the time. However, it was absent in 3 of our 11 patients, and in one (Case 8) there was no heart disease whatsoever. Apart from lowering of body potassium by the therapy employed for cardiac patients there is no doubt that heart failure itself may give rise to deficiency in cellular potassium. Biopsy studies of both cardiac and skeletal muscle have confirmed this (Talso *et al.*, 1953). Leakage of cellular potassium is induced in patients suffering from heart failure by anoxia, dehydration, acidosis, oedema, and anorexia, to mention but a few factors.

Differential Diagnosis

The bedside problem is threefold—namely, to suspect the presence of P.A.T.B.; to differentiate it from other arrhythmias; and, most important of all, to determine whether digitalis is the cause of it.

There is no specific syndrome due to the arrhythmia itself, which may last from several minutes to several weeks, and in our experience it is often the electrocardiogram which first reveals the condition, which sometimes has not been previously suspected. However, if careful inspection of the neck veins reveals a jugular a-wave faster than the apical rate the condition is suggested. It should be suspected also in any patient who is receiving digitalis if congestive heart failure suddenly worsens, or reappears, without other obvious cause. A ventricular rate which becomes quicker in spite of digitalis should suggest that an arrhythmia has appeared. A change in rhythm may be the clue—either sinus rhythm changing to an irregular rapid rhythm or atrial fibrillation suddenly giving way to a rapid regular rate. If, while any of these events takes place, the patient is receiving, in addition to digitalis, diuretics, especially chlorothiazide, or cortisone, or vomiting is present, the suspicion is increased. It has been emphasized that most patients are in congestive failure, but in our experience this fact is of little diagnostic help.

The electrocardiographic differential diagnosis of paroxysmal atrial tachycardia, when block is present, is between atrial flutter, atrial fibrillation, and nodal rhythm. If the block remits transiently the condition may be mistaken for sinus tachycardia.

The most common mistake is to confuse P.A.T.B. with atrial flutter, and, as we have emphasized, at times consideration of the electrocardiogram alone may not differentiate them, and indeed the one arrhythmia may merge into the other within the space of a minute or so. It is not the differentiation of flutter from P.A.T.B. which is paramount—the essential problem is to ascertain whether digitalis is the cause of the arrhythmia. The danger lies in mistaking P.A.T.B. for flutter and thereby incorrectly concluding that digitalis should be given.

Atrial fibrillation is also easy to confuse with P.A.T.B., particularly when the P waves in the latter condition are very small, or not visible, and the ventricular response is grossly irregular. At times long-standing atrial fibrillation can suddenly be replaced by P.A.T.B. and only an electrocardiogram reveals that this has taken place. On the other hand, if an increased dose of digitalis is thought to have induced atrial fibrillation, very careful search for P waves should be made, including, if necessary, the use of leads CR1, V3R, VE (ensiform lead), and even oesophageal leads.

If in P.A.T.B. a high degree of atrioventricular block is present and unvarying, and the P waves are not visible, it may be very difficult to differentiate electrocardiographically from nodal rhythm.

If the atrial rate in paroxysmal atrial tachycardia is in the region of only 150 a minute and 1:1 atrioventricular response is present, the disorder may be indistinguishable from sinus tachycardia. However, carotid sinus pressure will usually increase the degree of atrioventricular block in paroxysmal atrial tachycardia, at least for the time being, and this may be recorded simultaneously on a direct-writing electrocardiograph at the bedside. Other points of difference electrocardiographically are that, in sinus tachycardia, as the rate increases the P wave tends to increase in amplitude, whereas this does not occur in P.A.T.B., where the P is usually small in any case. The P–R interval in sinus tachycardia tends to be short, whereas in P.A.T.B. it is variable and may be prolonged.

The problem not infrequently arises in which a patient is admitted with P.A.T.B. and it is not certain whether this, in fact, is the result of digitalis overdosage or whether it constitutes an indication for intensive digitalis therapy. There is no doubt that occasionally P.A.T.B. can persist for long periods without digitalis ever having been given, and Schwartz and Levine (1950) report such a patient in whom the arrhythmia persisted almost continuously for 25 years. If the P.A.T.B. is accompanied by multifocal ventricular extrasystoles and sagging of the S–T segment it can be assumed that digitalis is the cause (Fig. 6).

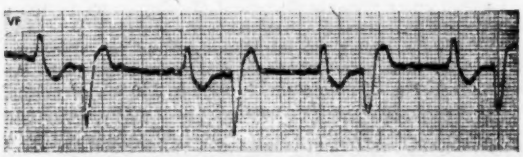

FIG. 6.—Lead VF. Paroxysmal atrial tachycardia with block, induced by digitalis. Atrial rate 115 a minute. Multifocal ventricular extrasystoles and S–T segment depression due to digitalis are present. Right bundle-branch block.

For patients where doubt exists whether or not digitalis has been responsible for the arrhythmia, Lown (1957) has introduced the intravenous acetyl-strophanthidin test. This is a means of deciding rapidly the degree of digitalization in the patient; but, particularly if the arrhythmia has been brought on by digitalis, the test is not without its dangers (Burgner and David, 1956), and indeed its fatalities, and we have no experience of it. The problem is an important one, and if doubt exists concerning the possibility of P.A.T.B. having been induced by digitalis we believe the following regime to be reasonable, and safer than the acetyl-strophanthidin test. First, carotid sinus stimulation is tried while a continuous direct-writing electrocardiogram is recorded. This simple manœuvre may stop the P.A.T.B. if it is not due to digitalis but will prove ineffective if digitalis is the cause (see Table III). Whether digitalis is the cause or not, the degree of atrioventricular block will be increased, but if the atrial rate is appreciably slowed the arrhythmia is very unlikely to have been induced by digitalis.

If the result of carotid sinus compression is inconclusive an injection of atropine may be tried. In both P.A.T.B. without digitalis and that induced by digitalis the degree of atrioventricular block usually decreases, but in that not due to digitalis the atrial rate

may quicken (Fig. 5 C), whereas it remains unaffected in the digitalis-induced type.

If doubt still exists procainamide or quinidine should be tried. They are commonly effective in P.A.T.B. without digitalis (Fig. 5 D) but less often if the P.A.T.B. is caused by digitalis. If they prove ineffective then potassium should be given—either by mouth or, if deemed urgent, intravenously in the dosage recommended below.

While these studies were being made we were fortunate to have admitted to our ward a patient who developed both P.A.T.B. and congestive heart failure while under observation but to whom no digitalis or diuretics had been given. We were thus able to observe how carotid sinus pressure, and the administration of atropine, potassium chloride, and procainamide, differed in their effects in this patient compared with those in whom P.A.T.B. had been induced by digitalis.

Case 12.—A woman of 76 was admitted to hospital after an attempted suicide with barbiturates. Three months previously an abdominal-perineal excision had been performed for carcinoma of the rectum. Twenty-four days after admission congestive heart failure developed with a rapid irregular pulse. An electrocardiogram showed an irregular atrial rhythm with at times a 2:1 block, the atrial rate being about 150 a minute (Fig. 5 A). No digoxin or diuretic therapy had been given. An iron-deficient anaemia of 57% was present and occult blood was found in the stools. One injection of mersalyl 2 ml. intramuscularly produced a diuresis of 90 oz. (2,550 ml.), after which the serum electrolytes (mEq/l.) were sodium 126, potassium 3.2, chloride 87, bicarbonate 30. The blood urea was 27 mg./100 ml.

Carotid sinus pressure decreased the atrial rate to 100 a minute and increased the A–V block to 3:1 (Fig. 5). Atropine 0.65 mg. was given intravenously and the atrial and ventricular rates were increased *pari passu* (Fig. 5 C). An infusion of 1 g. of potassium chloride in 540 ml. of normal saline was given over six hours. Serial electrocardiograms during this period showed no significant change. Oral potassium was then given, 9 g. daily over six days. The serum potassium rose to 5.5 mEq/l., but the electrocardiogram remained unchanged. After 400 mg. of procainamide intravenously normal sinus rhythm returned (Fig. 5 D). Although this was followed by 50 mg. of procainamide q.d.s. as a maintenance dose the heart rhythm continued to vary between regular sinus rhythm, sinus rhythm with atrial premature contractions, and atrial tachycardia with block.

Prognosis

Prognosis is said to be grave if P.A.T.B. is induced by digitalis. Of Lown's (1957) 64 patients, 37 (58%) were dead shortly after the onset of the arrhythmia. However, we consider that as many of his patients were already seriously ill with congestive heart failure, and as at times P.A.T.B. can be mistaken for atrial arrhythmias such as fibrillation and flutter where digitalis may be considered the drug of choice and even a small dose thus prove fatal, the mortality is almost certainly less than has been thought. Of our 11 patients only two died, and in one of them death followed suddenly 12 hours after mitral valvotomy (Case 4).

Lown *et al.* (1959) are of the opinion that the state of the myocardium rather than the dose of digitalis is critical for the development of intoxication, and think that severe cardiac disease or acute cardiac infarction lower the threshold to digitalis. While in general this is true, only one of our patients had evidence of cardiac infarction, and this was not recent. Seven were, or had been, in cardiac failure.

Treatment

Treatment should be started without delay, for if the arrhythmia is ignored ventricular tachycardia may supervene at any time and death may result from ventricular fibrillation. As a rule all that is necessary is to stop the digitalis and discontinue diuretics and cation-exchange resins, but if any potassium-losing state is present this must be dealt with as a matter of urgency. The renal mechanism for the conservation of potassium is less efficient than for sodium, and even starvation can cause a low potassium. In practice, however, there are only two causes of severe potassium deficiency—namely, intestinal and renal. Insufficient absorption of potassium from the gut may result from excessive purgation, from chronic diarrhoea, or from loss of intestinal fluid through vomiting or aspiration. We would point out that at times, if the potassium loss is great and digitalis is given, P.A.T.B. may be so induced in the absence of any heart disease, as happened in our patient (Case 8), in whom the serum potassium fell to 3.7 mEq/l. as a result of small-bowel obstruction treated by gastric aspiration and intravenous therapy. Renal loss of potassium occurs in massive diuresis, either therapeutically induced or resulting from uncontrolled diabetes, or from treatment with corticosteroids and A.C.T.H. In the absence of renal disease the acidosis of dehydration can *per se* produce loss of potassium via the kidney.

Unless extreme rapidity of potassium replacement is considered, vital potassium chloride should be given orally. The usual dose to begin with is 2 g. (1 g.=13 mEq), but, provided serious renal disease can be excluded, as much as 5 g. may be given as a starting dose if the serum potassium is greatly diminished. However, as we have said, a normal serum potassium does not imply that the cardiac potassium is also normal, and it is not a contraindication to potassium therapy. It is emphasized that frequent electrocardiographic control is important, and special care is indicated in elderly patients and those with severe congestive heart failure. If after four hours sinus rhythm has not appeared a further dose of 2 g. can be given, and this may be repeated as required. If the need is thought to be most urgent, and provided renal function is adequate, the potassium may be given intravenously. We found a strength of 1 g. to the pint (570 ml.) of 5% glucose in water effective in one of our patients (Case 8).

If serious renal disease is present and oral potassium fails then either procainamide or quinidine should be tried. They may be effective in paroxysmal atrial tachycardia induced by digitalis and that not so induced, but almost certainly more so in the latter. Owing to its tendency to cause a severe fall in blood-pressure, procainamide is probably best given orally in the first place, but if it proves ineffective by this route it can be given intramuscularly with an almost equally rapid effect to that of intravenous injection (Enselberg and Lipkin, 1952). The oral dose recommended is 1 g. followed by 0.5 g. six-hourly, and the intramuscular dose is 0.5 to 2 g. followed by 0.5 to 1 g. at intervals of several hours, depending upon the response. When quinidine was used we gave it by mouth.

As long ago as 1920 Zondek recognized the close relationship between digitalis, calcium, and potassium, and another treatment suggested for P.A.T.B. is lowering of the serum calcium by chelation. Like digitalis, the calcium ion alters the permeability of the cell membrane to sodium and potassium, and lowering of the serum

calcium may stop P.A.T.B. This can be achieved experimentally by sodium ethylenediamine tetra-acetic acid, which is a chelating agent with the property of binding calcium *in vivo* (Popovici *et al.*, 1950). Treatment of digitalis toxicity by this means has been employed by Gubner and Kallmann (1957). In our experience, however, stopping the digitalis preparation and diuretics, supplementing potassium, and preventing further potassium loss have always proved successful.

Summary

Although digitalis has been in use for over a century and a half and its toxic effects on the ventricles are well documented, its importance in the production of atrial arrhythmias has only recently been stressed. Of these, the commonest atrial disorder is P.A.T.B.

The potential seriousness of this arrhythmia when induced by digitalis is emphasized. Conditions which render the production of the arrhythmia likely, even with doses of digitalis that are small and have been unchanged for long periods, are discussed. The most important of these is a low myocardial potassium, the commonest cause of which is the use of diuretics.

We believe that P.A.T.B. is not a fixed specific entity, and that it merges into atrial flutter, from which at times it may be indistinguishable electrocardiographically or by any other means. Infinitely more important than trying to distinguish atrial flutter from P.A.T.B. is to determine whether digitalis is responsible for the arrhythmia. The problem of distinguishing P.A.T.B. due to digitalis from that arising without digitalis is discussed, and a regime is outlined by means of which it may be possible to differentiate them without submitting the patient to the risks of the acetyl-strophanthidin test.

The differential diagnosis is described in detail. We find the prognosis to be less serious than that usually stated; this is dependent upon the early recognition of the role of digitalis in precipitating the arrhythmia and stopping the drug immediately. Often no other treatment is necessary.

It has been claimed that serious myocardial disease with congestive heart failure is almost invariably present, but this was not so in our series; neither could we confirm the importance of fresh cardiac infarction as a precipitating factor. Details are given of a patient in whom no heart disease was present and yet in whom P.A.T.B. was induced by digitalis in the presence of a lowered serum potassium.

Although depression of the S–T segment was found in all patients, and ventricular premature beats in one-half of them, we wish to emphasize the uncommonness of other symptoms or signs of digitalis toxicity during the arrhythmia. Their absence cannot be taken as evidence that digitalis is not reponsible for the P.A.T.B. Estimation of the serum potassium may also be misleading, as it does not necessarily reflect the myocardial potassium, and the administration of potassium, therefore, should not be withheld because the serum estimation is normal.

Addendum.—Since this paper was submitted for publication we have had two further cases, thus emphasizing the increasing frequency of this arrhythmia. (1) A man aged 85 was admitted in congestive heart failure of ischaemic origin and in sinus rhythm. Digoxin, 0.25 mg. b.d., with mersalyl, 2 ml. I.M. twice a week, was given and sodium restriction maintained. One week later P.A.T.B. developed. Digoxin and mersalyl were discontinued and potassium chloride, 8 g. daily, was given by mouth. Four days later sinus rhythm was restored. (2) A woman aged 70 was admitted in gross congestive heart failure with P.A.T.B. She had received digitalis folia, ½ gr. (32 mg.) t.d.s., for 18 months, with mercaptomerin, 2 ml. twice weekly, and her sodium intake had been restricted. On her admission the serum potassium was 3.4 mEq/l. and the blood urea 40 mg./100 ml. Digitalis was reduced to ½ gr. (32 mg.) b.d., and she was given potassium chloride, 1 g. t.d.s. by mouth. Atrial fibrillation developed and has remained.

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ATRIAL TACHYCARDIA WITH ATRIOVENTRICULAR BLOCK DUE TO DIGITALIS POISONING

BY

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Digitalis can cause most types of cardiac arrhythmia. Ectopic beats (commonly ventricular), ventricular tachycardia, ventricular fibrillation, and heart-block are well-recognized manifestations of digitalis intoxication. It is not yet widely appreciated that atrial arrhythmias of various kinds may be caused by digitalis, and that one variety, atrial tachycardia with atrioventricular (A.V.) block, is almost always due to digitalis poisoning. This arrhythmia, which was first recognized as a complication of digitalis treatment by Sir James Mackenzie (1910), has received scant attention in this country, although several papers have been published about it in the United States during recent years (Lown and Levine, 1954, 1958; Goldberg, Bristow, Parker, and Ritzmann, 1958; Lown, Wyatt, and Levine, 1960).

The diagnosis of atrial tachycardia with atrioventricular block can be made only from the electrocardiogram. Clinically, its presence may be suspected

in a patient receiving digitalis who develops an increase in ventricular rate, usually regular, or whose initially high ventricular rate does not fall in the expected fashion. The atrial arrhythmia which it most resembles is atrial flutter, and the response to carotid sinus pressure is similar. The principal electrocardiographic criteria for the diagnosis were described by Lown and Levine (1954). These are an atrial tachycardia of not more than 250 per minute, a variable degree of A.V. block, and small upright P waves, particularly in lead I and lead II (Table I). Fig. 1 shows a typical example of this arrhythmia.

TABLE I.—*E.C.G. Features of Atrial Flutter and of Atrial Tachycardia with A.V. Block*

	Atrial Flutter	Atrial Tachycardia with A.V. Block
Atrial rate	250–350	120–250, usually 150–200
A.V. block	Usually 2: 1, 3: 1, 4: 1, or variable	All grades to A.V. dissociation
P wave	"Saw-tooth" in leads II and III	Upright and small in lead II
Isoelectric interval between P waves	Absent in lead II	Present in all leads
P–P interval	Unvarying	May be variable
Carotid sinus stimulation	Increase of A.V. block	Increase of A.V. block
Response to potassium	Does not restore sinus rhythm	Restores sinus rhythm if digitalis-induced

This paper reports 22 incidents which occurred in 19 patients of atrial tachycardia with A.V. block.

Results

Of the 19 patients with atrial tachycardia and A.V. block, seven had ischaemic, four had hypertensive, four had rheumatic, three had pulmonary, and one had congenital heart disease. Thirteen of these patients were over 50 years of age. Sixteen had congestive cardiac failure. Other details are given in Table II. Cases 1, 5, and 13 each had two separate episodes of atrial tachycardia.

Relationship to Digitalis.—Only one of these 19 patients had not received digitalis; he was recovering from a recent myocardial infarct. Before digitalis was started, 13 had sinus rhythm and two had atrial fibrillation; of the three remaining patients, two were thought to have atrial fibrillation, and one sinus rhythm, but electrocardiograms were not recorded. The smallest quantity of digitalis taken before the atrial tachycardia was recognized was 2.25 mg. of "digoxin" orally over three days. Two other patients had received less than 5 mg. of digoxin over the preceding four days. The rest had had digitalis in conventional maintenance doses for periods of up to 22 months. In two patients intravenous digoxin had been given shortly before the arrhythmia in addition to maintenance doses by mouth.

Relationship to Diuretics.—Before the onset of the atrial tachycardia, seven patients had received mersalyl, 10

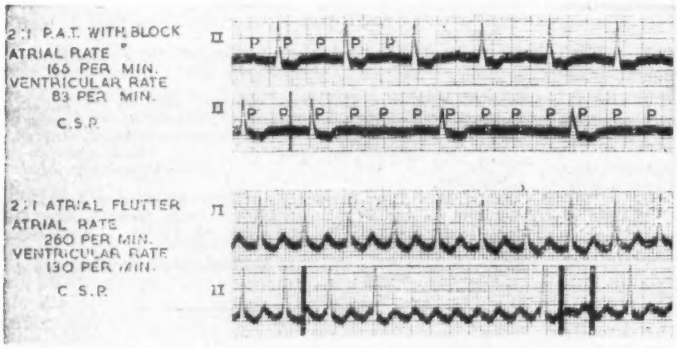

FIG. 1.—A typical example of digitalis-induced paroxysmal atrial tachycardia with 2:1 A.V. block. The response of this arrhythmia to carotid sinus pressure is similar to that of atrial flutter, an example of which is shown for contrast.

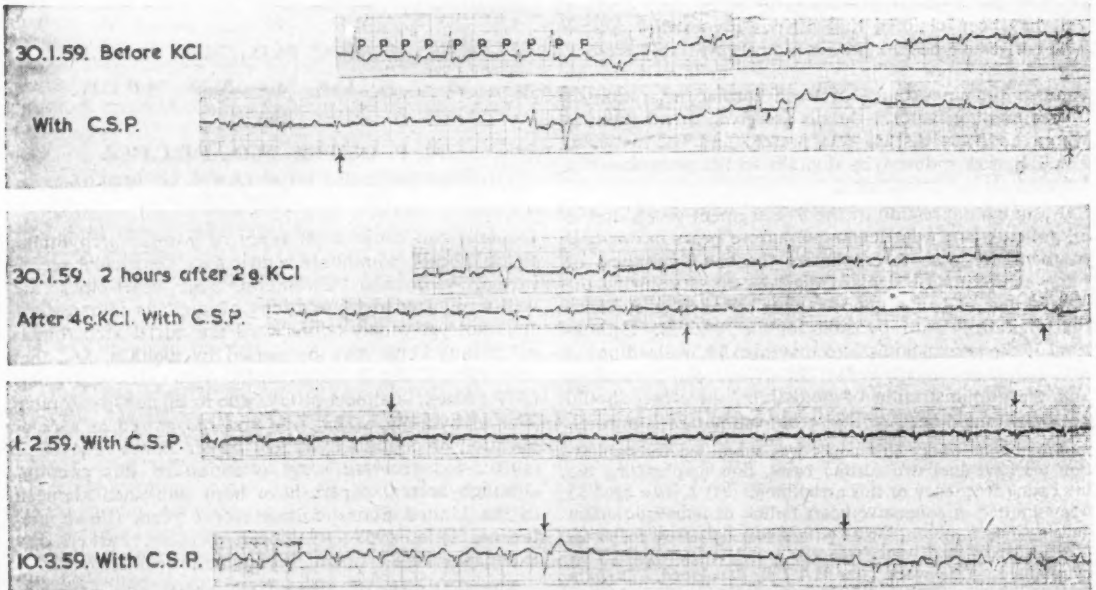

FIG. 2.—Another example of digitalis-induced atrial tachycardia with variable A.V. block. After carotid sinus pressure, 29 atrial contractions were recorded before A.V. conduction was re-established. The oral administration of potassium chloride rapidly restored normal sinus rhythm.

TABLE II.—*Details of 19 Patients with Atrial Tachycardia and Atrioventricular Block*

Case No.	Preceding Rhythm	Treatment Before Tachycardia	Atrial Rate	A.V. Conduction	Subsequent Rhythm	Remarks
1	Sinus	Digitalis leaf 386 gr. (25 g.) in 27 weeks. Mersalyl 2 ml. twice weekly for 27 weeks	152 136	2 : 1 2 : 1 and 1 : 1	Sinus ,,	Digitalis withheld when nauseated. Discharged taking digitalis. Died at home 1 month later
2	? A. fib.	Digitalis leaf 36 gr. (2·4 g.) in 3 days. Pot. iodide 1 g. thrice daily before and during A.T.	164 148	2 : 1 A.V. dissociation. Vent. rate 78	Atrial paralysis. Vent. rate 41 with periods of asystole	Died
3	Sinus. P–R 0·26 sec.	Digoxin 13 mg. over 7 days. 1 ml. mersalyl 4 days before	158	4 : 1 with vent. es. 1 : 1 with L.B.B.B.	No reversal observed	Died suddenly
4	Complete A.V. block or Wenckebach	None	213 213	A.V. dissociation. Vent. rate 71. 3 : 1	A. fib., later sinus	Recovering from acute myocardial infarction. Recovered from arrhythmia
5	A. fib.	Digoxin 8 mg. over 16 days. Mersalyl 4 ml.	160	2 : 1 and 1 : 1	Sinus	C.S.P. when in sinus rhythm produced A.V. block. Died in uraemia 4 months after second episode
	,, ,,	Digoxin 5 mg. over 14 days	200	A.V. dissociation. Vent. rate 120	,,	
6	Sinus	Digoxin 30 mg. over 9 weeks. Chlorothiazide 3 g. in 1 day. Mecamylamine	167–300 (one record)	A.V. dissociation. Vent. rate 68	No reversal observed	Digoxin continued after A.T. developed. No potassium given. Died 4 days after A.T. developed
7	,,	Digitalis leaf 19·5 gr. (1·3 g.) over 13 days. Digoxin 0·5 mg. I.V. on 15th day, A.T. on 16th day Mersalyl ? amount Chlorothiazide 16 g. over 3 weeks Pot. citrate 4 g. (one day)	136	1 : 1 with long P–R interval and Wenckebach periods	Sinus	Digoxin stopped and pot. citrate continued after A.T. developed Glucose and insulin also given Recovered
8	? A. fib.	Digoxin ? 17·5 mg. over 5 weeks	200	2 : 1 with coupled vent. es.	Sinus 2 hours after KCl	Recovered. Remained sensitive to C.S.P. 12 weeks after last digoxin given (A.V. block with ventricular escape; A.V. dissociation)
9	Sinus	Digoxin in unknown maintenance dose for 1 year Chlorothiazide in unknown amount for 1 year	115 213 167	1 : 1 P–R 0·22 sec. A.V. dissociation. Vent. rate 120 1 : 1	Sinus	Digoxin 0·5 mg. I.V. and 0·25 mg. t.i.d. orally after A.T. developed. Pot. chloride 8 g. orally over 2 days. Died on day sinus rhythm returned
10	,,	Digoxin 8·25 mg. over 15 days Mersalyl 14 ml. over 14 days	230 136	2 : 1 multiple vent. es. A.V. dissociation, multiple vent. es.	,,	Mersalyl-resistant oedema prior to A.T. No further episode despite continued digoxin, chlorothiazide, and prednisolone
11	,,	Digoxin 2·25 mg. over 3 days. Hydroflumethiazide 600 mg. over 2 weeks	125 115	Wenckebach periods 1 : 1 P–R 0·28 sec. (3 days later and no digoxin)	Sinus with long P–R interval. Later sinus tachycardia with normal P–R interval	Digitalis stopped and pot. citrate given when A.T. developed. Death 12 days later. S.B.E. and pyrexia possibly contributed to tachycardia
12	A. fib.	Digitalis maintenance 4 years 3·5 mg. digitalin orally. Mersalyl 8 ml. Chlorothiazide 16 g. Pot. citrate 84 g. within preceding 20 days. 2·75 mg. digoxin I.V. within 7 days	150 160	A.V. dissociation with R.B.B.B. Complete A.V. block	No reversal observed	Died in attack of A.T. with complete A.V. block Given calcium gluconate for tetany before the onset of complete A.V. block
13	Sinus	Digoxin 59·75 mg. over 83 days. Chlorothiazide 18 g. over 36 days. Pot. citrate 210 g. over 35 days. Low-sodium diet	142 130	2 : 1 or 1 : 1 1 : 1 P–R 0·24 sec.	Sinus ,,	Died 2 days after second attack of A.T. Each attack ended after 4 g. of KCl given by mouth. Between 1st and 2nd attacks digoxin had been restarted and a big diuresis had occurred
14	Sinus with supravent. es.	Digoxin in unknown maintenance doses for several weeks Digoxin 0·75 mg. daily for at least 1 month Chlorothiazide 22 g. over 39 days	150 214 200	A.V. dissociation. 2 : 1 A.V. dissociation. Vent. rate 60	,,	A.T. lasted 11 days. Reversion occurred despite continuance of digoxin and chlorothiazide
15	Sinus	Digoxin 21·5 mg. over 7 weeks Chlorothiazide 64 g. over 8 weeks	152	2 : 1 P–R 0·28 sec.	Complete A.V. block	Poorly controlled diabetes, with vomiting, before admission. Died
16	,,	Digoxin 30 mg. orally in 40 days Chlorothiazide 84 g. over 14 weeks Mersalyl 96 ml. over 24 weeks Pot. chloride 414 g. over 42 weeks Thyroid extract 22·5 g. over 1 year	176	2 : 1 P–R 0·24 sec.	Not observed	Died 3 weeks after arrhythmia discovered. Digoxin had been continued (3·75 mg. week) with mersalyl and KCl. Duration of A.T. unknown
17	Unknown	Digoxin 4 mg. orally over 4 days Mersalyl 2 ml. I.M. 2 days before	125 150 125	1 : 1 P–R 0·24 sec. 1 : 1 P–R 0·28 ,, 1 : 1 P–R 0·32 ,,	No reversal	Died 4 days after A.T. first noted still taking digitalis. Before A.T. had frequent vomiting with dehydration. ? Nutritional deficiency. Diabetic ketosis
18	Sinus	Digoxin 3·5 mg. orally in 4 days	166	2 : 1	Sinus	Digitalis was stopped and KCl 1 g. 2-hourly begun when A.T. first noted. Died 5 days later in sinus rhythm
19	,,	Digoxin 255 mg. in 22 months Chlorothiazide 3 g./week for 10 months	230 230	2 : 1 2 : 1	,,	Digitalis stopped 7 days after A.T. first noted and KCl 3 g./day started. Next day S.R. was restored. Recovered

es. = extrasystoles. supravent. = supraventricular. vent. = ventricular. A.T. = atrial tachycardia. R. or L.B.B.B. = Right or left bundle branch block. C.S.P. = carotid sinus pressure. S.B.E. = subacute bacterial endocarditis.

chlorothiazide or hydroflumethiazide, and three mersalyl and chlorothiazide. Five of the 10 patients who were given chlorothiazide or hydroflumethiazide also had regular doses of potassium.

Electrolyte Disturbances.—Serum electrolyte concentrations were estimated in eight patients when the arrhythmia was recognized. In three there was a definite reduction of sodium, potassium, or chloride concentrations.

Outcome.—The immediate outcome is shown in Table III. Of eight patients who continued to take digitalis, six died without reverting to sinus rhythm. When digitalis was stopped, nine out of ten patients regained sinus rhythm; three of these ten did not receive potassium, and one of the three died before regaining sinus rhythm.

TABLE III.—*Outcome in 18 Patients with Digitalis-induced Atrial Tachycardia with A.V. Block*

	Reverted to Sinus Rhythm	Died Without Observed Return to Sinus Rhythm
Digitalis stopped. K not given	2	1
" " given ..	7	—
Digitalis continued. K not given	1	5
" " given ..	1	1

Effect of Carotid Sinus Stimulation.—Compression or massage of one or both carotid sinus areas was carried out in eight patients. In six the degree of A.V. block was increased: an extreme example, with 29 unconducted beats during carotid sinus stimulation, is shown in Fig. 2. In one patient there was a change in the form of the P wave without alteration in the degree of block. There was a slight decrease in the atrial rate in some cases, but in none was the arrhythmia abolished. In the remaining patient carotid sinus stimulation was ineffective. After sinus rhythm had been restored and digitalis stopped, carotid sinus stimulation continued to produce atrioventricular block in several of these patients (Fig. 2). In one patient this effect could still be produced four and a half months after withdrawal of digitalis.

Discussion

Atrial tachycardia with A.V. block appears to have been caused by digitalis in 21 of the 22 incidents reported here. Of 112 episodes of this arrhythmia reported by Lown (1957), 83 were caused by digitalis and in only 13 could the drug be exonerated. Thus atrial tachycardia with A.V. block is usually a complication of digitalis administration. Its incidence is difficult to assess. Thirteen of our cases were recognized during the last 18 months, usually during routine reporting of electrocardiograms. We have been unable to arrive at an estimate of the number of patients at risk during this period.

The recognition of tachycardia in a patient receiving digitalis is often regarded as an indication for increasing the dose of digitalis. If atrial tachycardia with A.V. block is the cause of a high ventricular rate, the giving of more digitalis may be lethal. Digitalis poisoning is likely to have been the immediate cause of death in eight patients (Cases 1, 2, 3, 6, 12, 15, 16, and 17), but digitalis cannot be incriminated with certainty in their deaths, since these eight patients had either cardiac failure or recent myocardial infarction at the time their arrhythmia began. Atrial tachycardia with A.V. block is particularly likely to develop in patients who already have serious heart disease.

Diagnosis

The main criteria for the diagnosis of atrial tachycardia with A.V. block have been stated. When the atrial rate is less than 150 a minute there is usually 1:1 A.V. conduction. Rates greater than 150 a minute are usually associated with 2:1 or higher grades of block. The degree of block may vary from a long P–R interval to A.V. dissociation. Pressure on the carotid sinus nearly always increases the degree of A.V. block, and may temporarily stop A.V. conduction, with little or no slowing of the atrial tachycardia. This response to carotid sinus stimulation is like that seen in atrial flutter and unlike that usually seen in paroxysmal atrial tachycardia. It is of great value in confirming the diagnosis. In several of the cases here described P waves were obscured in the QRST complex. When this happens in the presence of 2:1 A.V. block, atrial tachycardia can easily be overlooked (Fig. 3).

Atrial tachycardia with A.V. block may be confused with atrial flutter, for the two possess many features in common and it may be impossible to distinguish them with certainty. Their chief features are summarized in Table I. The characteristic "saw-tooth" baseline of atrial flutter is most pronounced in leads II and III and may not be seen in other leads; thus leads II and III are the leads upon which the distinction is most reliably made. In atrial tachycardia, however, P waves are often best recognized in the right chest leads. It is impossible to tell digitalis-induced atrial tachycardia with A.V. block from sinus tachycardia due to

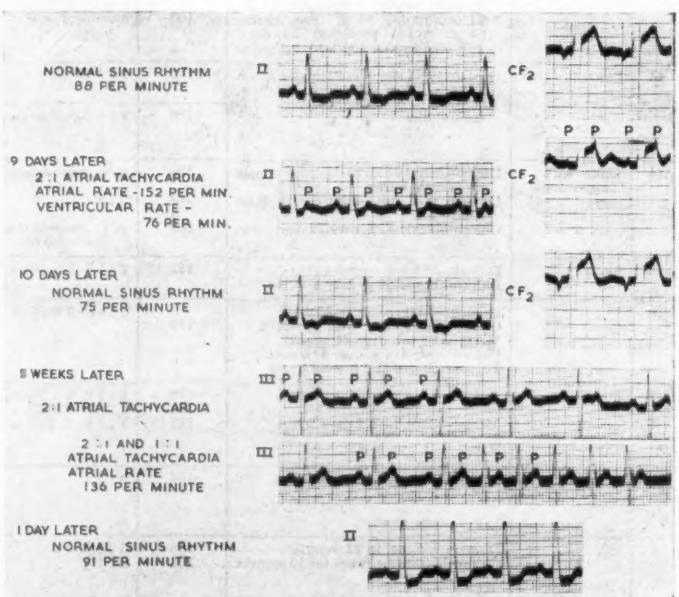

FIG. 3.—A further example of digitalis-induced atrial tachycardia with 2:1 and 1:1 A.V. block The P waves are superimposed on the T waves.

some other cause associated with a long P–R interval induced by digitalis, unless there has been a clear-cut alteration in the shape of the P wave.

Potassium Depletion

Like other digitalis-induced arrhythmias, atrial tachycardia with A.V. block is especially prone to occur in the presence of potassium depletion. Cardiac failure is associated with cellular potassium depletion, and potassium salts given by mouth (even if absorbed) do not always prevent great losses of this ion during treatment with diuretics. The incidence of atrial tachycardia with A.V. block may be increasing since the introduction of chlorothiazide. In 10 of the 14 cases which have been observed since 1958, chlorothiazide or hydroflumethiazide had been given before the development of atrial tachycardia with block. The danger of these drugs seems to lie partly in the ease with which they can be given compared with injections of mercurial diuretics and partly because of the considerable potassium loss which they produce. Determinations of serum electrolyte concentrations were not made in all the cases under review. Of eight cases in which they were made, five showed no abnormality of sodium, potassium, or chloride concentration. Severe cellular potassium depletion may be present with normal serum concentrations of these ions. Most of the patients in this series probably had potassium deficits of some degree resulting from cardiac failure, diuretics, sodium restriction, vomiting with dehydration, poorly controlled diabetes, or various combinations of these.

Prognosis and Treatment

Patients who develop digitalis-induced atrial tachycardia with A.V. block have a poor prognosis. Of the 18 patients in this series, 13 died within four months of the occurrence of the arrhythmia. In five of these, digitalis intoxication was not directly responsible for death. Patients who develop atrial tachycardia with block are already gravely ill, and it is difficult to assess the role of the various factors involved in their rapid deterioration. Although the tachycardia itself may be important in accelerating the downhill course, resistant cardiac failure with electrolyte imbalance and the other toxic effects of digitalis also contribute. The development of this unusual and almost specific arrhythmia may serve as a timely warning of the presence of potassium deficiency and digitalis poisoning. Its prompt treatment may lead to a striking improvement in the patient's general condition and in his response to diuretics.

It is apparent, on theoretical grounds and from practical experience, that both the administration of potassium and the withdrawal of digitalis are essential for the treatment of digitalis-induced atrial tachycardia with A.V. block. The rapid effects of oral potassium are illustrated by Fig. 2, which is representative of other cases, and by the experience of Lown, Wyatt, and Levine (1960), and of Oram, Resnekov, and Davies (1960). Potassium is rapidly absorbed when given by mouth. The dose required to correct the arrhythmia ranges, in our experience, from 2 to 8 g. of potassium chloride. When necessary, 40 mEq of potassium (3 g. of potassium chloride) may be given as an intravenous infusion lasting an hour or two, under continuous electrocardiographic control (Lown *et al.*, 1960). Potassium chloride may have advantages over other potassium salts, since hypochloraemic alkalosis is commonly present in these patients.

If this treatment is undertaken the prognosis for the arrhythmia is good. The subsequent management of congestive heart failure, which is so often present, may, however, present difficulties. A potassium supplement should be given whenever diuretics are administered. Digitalis is not necessarily contraindicated provided potassium is administered at the same time; several of the patients here reported were treated with digitalis after successful management of digitalis-induced atrial tachycardia with block and the arrhythmia did not recur.

Although the prophylactic administration of potassium might prevent the development of atrial tachycardia with A.V. block, the arrhythmia can arise in spite of this precaution. Indeed, in retrospect, we would raise few objections to the treatment received by many of our patients before the development of atrial tachycardia with A.V. block. It is all the more important, therefore, that physicians should be alert to this complication of digitalis therapy.

Summary

Twenty-two episodes of atrial tachycardia with atrioventricular block have been observed in 19 patients with various types of advanced heart disease. Eighteen of these patients were receiving digitalis.

Atrial tachycardia with A.V. block is a serious complication of digitalis treatment which is often overlooked or confused with atrial flutter. It is probably increasing in incidence as a result of the widespread use of potassium-depleting diuretics.

Awareness and recognition of digitalis-induced atrial tachycardia with A.V. block is important, since it responds rapidly to withdrawal of digitalis and the administration of potassium.

We are grateful to Professor Sir Derrick Dunlop and Dr. Rae Gilchrist for their advice and encouragement, and to them, and other physicians in the Edinburgh Royal Infirmary, for permission to report cases under their care.

[ADDENDUM.—Six additional episodes of atrial tachycardia with A.V. block have been observed in six patients during the last three months. All had received digitalis before the arrhythmia began, but in one the drug was probably not responsible. Digitalis was continued in four, of whom three died, two without reversion to sinus rhythm.]

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In 1959 there were 30 fatal accidents and 7,000 other reportable accidents in the shipbuilding and ship-repairing industry in Great Britain, and a number of typical occurrences which have been notified to H.M. Inspectors of Factories are included in the latest edition of *Accidents—How they happen and how to prevent them*, which has recently been published (No. 44, H.M.S.O., price 1s. 3d. net).

VIROLOGICAL STUDIES IN NATURAL COMMON COLDS IN SHEFFIELD IN 1960

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It has been known for several years that certain nasal washings derived from people with natural common colds were capable, on serial passage through human volunteers, of producing an experimental infection resembling coryza in a variable number of cases (Andrewes, 1949; Roden, 1958). Hitchcock and Tyrrell (1960) and Tyrrell and Parsons (1960) have shown that nasal washings capable of transmitting infection produced interference with known viruses or cytopathic changes in tissue cultures grown under rather unusual environmental conditions—that is, low temperature and low bicarbonate concentrations. Studies with these viral agents showed that they bore a definite aetiological relation to the experimental disease under study. There appeared to be two distinct categories of this "Salisbury" group of viruses, one producing cytopathic change only on human embryonic kidney tissue, the other producing changes on both human embryo and rhesus monkey kidney cultures.

These findings are of undoubted importance in the interpretation of trials on human volunteers in a defined experimental model infection. However, the relevance of these studies to the aetiology and epidemiology of natural common colds in the community at large can be evaluated only if it can be shown that viruses akin to the Salisbury group can be isolated direct from natural infections at the present time in other localities, or that serological evidence can be obtained to show that such viral agents have a definite role in "wild" colds.

The purpose of the present communication is to report the isolation from cases of natural common colds in Sheffield in January–June, 1960, of cytopathic agents closely resembling the prototype Salisbury strains in their biological characteristics.

Materials and Methods

Tissue Cultures

Monkey kidney (M.K.) cultures were obtained from immature rhesus monkeys (4–6 months old). Human embryo kidney (H.E.K.) cultures were derived from specimens obtained either by hysterotomy or by spontaneous abortion between the 12th and the 28th week of gestation. The preparation of primary tissue cultures from each source was essentially similar. The renal cortex was chopped into small fragments and washed repeatedly in phosphate-buffered saline (P.B.S.) containing 1,000 units each of penicillin, streptomycin, and polymyxin B. A dispersed cell suspension was prepared by incubation at 37° C. with stirring in serial aliquots of trypsin (0.25% "Difco" 1/250 trypsin in P.B.S.). The final washed cell mass was suspended in growth medium at a concentration of 1 ml. of packed cells per 250 ml. of medium. (This is roughly equivalent to 10^5 cells per ml., but, since optimum suspensions are those containing small clumps rather than single cells, quantitation with counting-chambers is of no great value.)

The cell suspensions were distributed in 1-ml. amounts in 6 by 5/8 in. (15 by 0.6 cm.) "pyrex" test-tubes with silicone bungs or in 50-ml. amounts in 20-oz. (570-ml.) medical flat bottles. Large semiconfluent islets of epithelial tissue were present four to five days after distribution and most cultures were fully confluent by the seventh day. When required for virus inoculation the growth medium was exchanged for 1-ml. amounts of maintenance medium.

Secondary cultures of monkey kidney tissue were made either from bottles of primary tissue prepared as above, or from similar preparations (Mair and Tobin, 1960) kindly provided by the Department of Biological Standards, National Institute of Medical Research, London. The primary cell sheet was dispersed by trypsinization, the cell concentration adjusted to approximately 10^4 cells/ml. in growth medium, and distributed into tubes. In most cases semiconfluent growth was obtained within 48 hours.

Bottle cultures of M.S. (Tytell strain) (Kanda and Melnick, 1959), H.EpII (kindly provided by Dr. R. Chanock, National Institute of Allergy and Infectious Diseases, Bethesda, Maryland, U.S.A.), and HeLa (Tomlinson strain) were dispersed by trypsinization and dispensed into tubes at a concentration of 5×10^4 cells/ml.

Media

Growth medium for H.E.K. and for primary and secondary M.K. cultures consisted of Hanks's saline (with 0.35 g. of sodium bicarbonate per litre) 85%; heated calf serum, 5%; and lactalbumin hydrolysate, 10% of 5% stock solution in Hanks saline. In this and all other media penicillin 100 units, streptomycin, polymyxin B, and nystatin 100 μg./ml. were incorporated.

Standard maintenance medium (E.M. medium) consisted of Earles saline with 2.2 g. of bicarbonate per litre, 93%; plus 2% heated calf serum and 5% lactalbumin solution.

For experiments with common cold viruses the medium consisted of Hanks's saline plus 2% calf serum and 5% lactalbumin hydrolysate solution. In preliminary experiments the bicarbonate concentration of the medium was 0.35 g./l.; in later isolation and passage experiments this was increased to 0.52 g./l. In this latter medium ("C.C." medium), the appearance and survival time of tissue culture sheets was much better without any apparent loss of susceptibility to the standard H.G.P. strain of Salisbury viruses.

HeLa cultures were grown in Hanks's saline containing 20% calf serum and 10% lactalbumin solution; M.S. cells were grown in "199" medium (0.88 g. of bicarbonate (Glaxo) per litre) containing 10% calf serum, and H.EpII cells in M.K. growth medium.

Clinical Specimens

Nasal washings were obtained by instilling into each nostril 199 medium containing 1,000 units of antibiotics per ml. and getting the patient to snort out into a wide-mouthed sterile jar; 5–10 ml. of washings was collected from each case. After homogenization in a mechanical blender and centrifugation at 1,500 r.p.m. for 10 minutes the material was divided into small tubes and stored at −70° C. until used. Throat or nose swabs were

obtained on stick pledgets, broken off into 5 ml. of 199 medium, and homogenized and centrifuged as for nose washings before storing. Samples were taken on the first day of coryza and repeated 10 to 15 days after the symptoms had subsided.

Inoculation of Specimens

0.2–0.3 ml. of material was inoculated into each of 4 H.E.K. and M.K. tubes containing C.C. medium, and incubated at 33° C. with constant rolling ("C.C." conditions); the tubes were selected one to two days before full confluence. Additional inoculations were made into M.K. and H.E.K. tubes containing E.M. medium incubated without rolling at 37° C. ("routine diagnostic" conditions). All attempted isolations from clinical material were segregated strictly from passage experiments with known viruses. All tubes were observed daily for cytopathic changes, and at intervals of two to three days for haemagglutination or haemadsorption (Vogel and Shelokov, 1957) with human group O red cells. Tissue-culture fluids were changed as indicated by fall in *p*H; fluids harvested on the fourth to sixth day were used for passage to further cultures, but each tube was observed for 14 days before concluding that cytopathic effect was absent.

To guard to some extent against picking up "wild" agents from the tissues themselves on serial passage, fluid from uninoculated tubes of each batch of tissue employed has been passed serially through each subsequent batch. No cytopathic or haemadsorption agents have appeared as a result of this control manœuvre.

Neutralization Tests

Initial 1/5 dilutions of all sera in 199 medium were inactivated at 56° C. for 30 minutes before further serial dilution in 199. Virus seed cultures were diluted where necessary in 199 to a concentration of 100 TCD_{50} per 0.1 ml. Aliquots of virus and serum dilutions were incubated for 3 hours at 37° C., and 0.2 ml. of each mixture was then inoculated into each of four H.E.K. or M.K. tubes incubated under C.C. conditions. Tubes were scored daily for 14 days for cytopathic effect. Normal human or rabbit sera were included in each batch of tests.

Standardization of Methods

Before embarking on a study of the viral aetiology of natural common colds it seemed essential to investigate the sensitivity and selectivity of the present tissue-culture techniques, based on those used by Tyrrell and Parsons (1960).

Cultures of the prototype Salisbury virus H.G.P. and immune rabbit anti-H.G.P. serum were kindly provided by Dr. D. A. J. Tyrrell. The method of preparation of this antiserum will be described (Tyrrell, 1960); in end-point neutralization tests with 100 TCD_{50} of virus per ml. a titre of approximately 1/200 was obtained.

Reproducible cytopathic effects, similar to those described by Tyrrell and Parsons (1960) were obtained on both M.K. and H.E.K. tissue cultures under C.C. conditions; no cytopathic change occurred in parallel cultures under "routine diagnostic" conditions. Serial passage of the cytopathic agent was successful through each batch of M.K. and H.E.K. tissue used in the subsequent experiments. Cytopathic effect began within three to five days of inoculation and proceeded from discrete well-demarcated virus plaques to complete cell-sheet degeneration in four to five days; peak titres of virus in harvested tissue-culture fluid were approximately 10^3 TCD_{50}/ml.

To determine whether these cultural conditions were equally satisfactory for primary isolations of "common cold" viruses from human material a small-scale volunteer experiment was performed.

Seven medical students, continuing to work in their normal environment, were given intranasal instillations of 0.5 ml. of a 1/10 dilution of a known H.G.P. virus stock (provided by Dr. Tyrrell); seven similar students were given non-infected material. This and subsequent human volunteer studies will be reported elsewhere. Two students developed typical coryza; both were in the virus-inoculated group. From nasal washings taken on the first day of illness (five days after inoculation) a cytopathic agent was isolated both on M.K. and H.E.K. tissue-cultures under C.C. conditions. No cytopathic change occurred in M.K. and H.E.K. under routine diagnostic conditions at 37° C. after inoculation either of original nasal washings or of positive culture fluids harvested from tubes incubated at 33° C. A repeated nasal lavage from these two volunteers after complete recovery from coryza did not contain demonstrable virus.

The two virus strains obtained were neutralized specifically by anti-H.G.P. rabbit serum: pre-infective sera from the two individuals (cases 47/60 and 53/60) did not neutralize either of the viruses or the standard H.G.P. strain, whereas convalescent serum samples neutralized both H.G.P. virus and the two isolates (H.G.P./47/60 and H.G.P./53/60) to similar titre.

The selectivity of C.C. conditions was investigated by parallel inoculation of M.K. and H.E.K. cultures under C.C. and routine diagnostic conditions with stock cultures of various known respiratory viruses in concentrations varying from 10^{-1} to 10^{-4} dilutions of tissue-culture fluid pools. The test viruses included influenza A/Jap/305/EFME, parainfluenza 1 (Sendai), parainfluenza 2 (C.A. virus, Firth strain), parainfluenza 3 (H.A.1), R.E.O. type 1 (Echo type 10 prototype strain), adenovirus type 2, Coxsackie type B4, and herpes simplex virus. All tubes were examined daily for cytopathic effect, and in the case of the myxoviruses tubes showing no cytopathic change were examined by haemadsorption. In all cases similar virus replication occurred under both sets of cultural conditions.

These findings suggest that, although optimal cultural conditions for common-cold viruses involve lower temperatures and lower *p*H than for most respiratory viruses, infections caused by known myxoviruses, etc., are not likely to be missed on examining clinical specimens under C.C. conditions.

Investigations with Clinical Material

Twenty-five persons with typical coryza were investigated; 18 patients suffering from various mild upper respiratory tract febrile infections were similarly examined, and 8 normal people with no respiratory symptoms over the previous 10 to 20 days were also included. Nasal washings and throat swabs or sputum, where available, were inoculated into M.K. and H.E.K. tissue under C.C. and routine diagnostic conditions as described above. In most cases one or two blind passages were made from the fluids of negative primary inoculations, but in no case did this procedure

reveal cytopathic agents. The virus isolations from primary inoculations are summarized in Table I.

TABLE I.—*Virus Isolations from Nasal Lavage and Throat Swabs Under Various Cultural Conditions*

Type of Case	No. of Cases Tested	No. of Positive Isolations			
		Cultures at 33° C. C.C. Conditions		Cultures at 37° C. Routine Conditions	
		M.K.	H.E.K.	M.K.	H.E.K.
Coryza	25	1*	8	0	0
Infection of upper respiratory tract	18	2†	2	2	2
Healthy individuals	8	0	0	0	0

* This isolate (30/60) was also isolated on H.E.K. at 33° C.
† Adenovirus type 3 was isolated from two cases under all cultural conditions.

No cytopathic or haemadsorption agents were isolated from any of the nasal specimens from normal people. From the assorted respiratory infections adenovirus type 3 was isolated from two cases under both C.C. and routine diagnostic conditions; no other cytopathogenic or haemadsorption agents were found.

From 8 of the 25 persons with natural common colds, cytopathic agents were isolated on H.E.K. incubated under C.C. conditions; in only one of these (Case 30/60) was primary virus isolation also made on M.K. under C.C. conditions, and in no case did cytopathic changes occur in cultures under routine conditions at 37° C.

Duplicate nasal washings from 9 cases were transported in CO_2 ice to the Common Cold Research Unit, Salisbury. In blind tests, virus isolations were achieved in all five of the specimens found to be positive in this laboratory (Tyrrell, personal communication).

The properties of virus strains 30/60 and 16/60 have been investigated in more detail than other isolates, and these results will be described separately.

Virus 30/60

The patient was a 20-year-old female office worker. From nasal washings on the first day of coryza, virus was isolated both on H.E.K. and M.K. tissue under C.C. conditions and from throat swab on H.E.K. The virus was successfully reisolated from these sources after six months' storage at approximately −70° C.

The first virus generation derived from H.E.K. and that from M.K. could be propagated equally readily on either tissue under C.C. conditions with similar cytopathic changes, like those of H.G.P. virus; no haemagglutination or haemadsorption was detected. The fifth virus generation on either tissue remained equally capable of cross-propagation.

No cytopathic effect was obtained by inoculation of the first to fifth generations of virus into M.K. or H.E.K. at 37° C, either rolled or stationary, in either E.M. or C.C. medium.

Quantitative growth studies with 30/60 virus remain incomplete. Preliminary experiments, however, using cytopathic changes as the sole criterion, have helped to establish certain growth characteristics. In early passage experiments it was found that the greatest chance of successful propagation (and hence, presumably, peak virus titre) is from tissue-culture fluids harvested three to four days after inoculation, well before widely disseminated cytopathic change occurs. Fluids harvested after 50% of maximum cytopathic effect (six to nine days) have proved extremely unreliable for serial passage.

Infectivity titres of 30/60 virus propagated under C.C. conditions have remained low (approximately 10^3 TCD_{50}/ml.) up to the fifth virus generation.

There were no obvious differences in growth with bicarbonate concentrations varying from 0.35 to 0.88 g./l., calf serum concentrations from nil to 2%, or with change from Hanks-lactalbumin medium to 199. Cytopathic effects progressed uniformly from small discrete plaques to confluent degeneration only in tubes where the *p*H did not fall significantly below *p*H 7. At lower *p*H, where either the medium was left unchanged beyond five days or the bicarbonate concentration was reduced below 0.35 g./l., cytopathic changes ceased to advance; no secondary virus plaques appeared and the early focal lesions regressed.

In M.K. tubes incubated at 33° C. in C.C. medium no cytopathic change was observed over 14 days' stationary incubation after inoculation of 0.2 ml. of undiluted fluid of third-generation 30/60 virus. M.K. or H.E.K. cultures inoculated from 5 to 17 days after seeding approximately 10^5 cells per tube showed similar cycles of cytopathic change, suggesting that the age of the cell sheet is not critical for susceptibility to 30/60 virus; propagation on primary M.K. cultures has been as reproducible as with secondary cultures. H.E.K. cultures derived from embryos 12–28 weeks old proved equally susceptible to 30/60 virus, but one batch of kidney tissue from a 3-day-old child produced no cytopathic change with this virus or with strains 16/60, 1/60, or 20/60; fluids harvested from these cultures did not produce cytopathic changes on passage to further H.E.K. or M.K. batches.

The cell sheets of this baby kidney were perfectly normal in all growth characteristics, and primary isolations of adenoviruses were made on this tissue. In similar experiments with H.G.P. virus (Flewett, personal communication) no cytopathic effect occurred on human neonatal kidney tissue, though concurrent inoculations of M.K. and H.E.K. tubes demonstrated normal virus growth.

The biological characteristics of 30/60 virus appear superficially similar to those of H.G.P. virus, but cross-neutralization experiments (Table II) suggest that the

TABLE II.—*Cross-neutralization Tests on H.E.K. Cultures with Viruses Isolated from Coryza*

Virus Strain	Rabbit Anti-H.G.P. Serum	Paired Sera from Cases of Coryza						Rabbit Anti-16/60 Serum	Normal Rabbit Serum
		53/60		30/60		16/60			
		A	C	A	C	A	C		
H.G.P.	+	0	+	−	−	−	−	−	0
H.G.P./53/60	+	0	+[1]	0	0	0	0	0	0
30/60	0	0	0	0	+	0	0	0	0
16/60	−	0	0	−	0	0	+[2]	+[3]	0

\+ = Neutralization of virus at 1/10 serum dilution.
0 = No neutralization.
− = Untested.
A = Acute illness serum sample.
C = Convalescent serum sample.
[1] In subsequent titration, neutralization titre = 1/40.
[2] In subsequent titration, neutralization titre = 1/20.
[3] In subsequent titration, neutralization titre = 1/80.

two viruses are serologically different from each other and from viruses isolated only on H.E.K.

Virus 16/60

The patient was a female house-physician in another Sheffield hospital; there was no contact with the virus laboratory. From nasal lavage on the first day of coryza a cytopathic agent was isolated on H.E.K. under

C.C. conditions. After six virus generations through H.E.K. cytopathic effects regularly began within 48 to 72 hours after inoculation and proceeded to full degeneration by six to seven days. As with 30/60 virus, efficiency of passage decreased sharply in culture fluids harvested beyond the 50% level of cytopathic change. The peak titre of the sixth virus generation was approximately 10^4 TCD_{50}/ml.; cytopathic change occurred only on incubation at 33° C. in low bicarbonate medium, but rolling did not seem to be essential.

No cytopathic agent was isolated from the nasal washings on primary inoculation of M.K. tubes under C.C. conditions nor on two subsequent blind passages.

The third virus generation was inoculated into suckling mice intracerebrally and subcutaneously and into adult mice and weanling hamsters intranasally without obvious pathological effect.

In neutralization tests with 100 TCD_{50} of fourth-generation 16/60 virus per 0.1 ml. (Table II) a rise in antibody titre from <1 in 5 to 1 in 20 was demonstrated with paired sera from Case 16/60. No inhibition occurred with two samples of normal human serum or normal rabbit serum. There was no neutralization by animal or human anti-H.G.P. sera; conversely, convalescent serum of Case 16/60 at 1 in 10 dilution failed to neutralize H.G.P. or 30/60 virus.

An immune antiserum against 16/60 virus was prepared in rabbits by a multiple-depot-antigen technique (Hayward and Augustin, 1957). The antigenic material was obtained by fluorocarbon purification (Epstein, 1958) of 200 ml. of tissue-culture fluid from the fourth H.E.K. generation, concentrated tenfold in the Spinco L model centrifuge at 40,000 r.p.m. for 45 minutes.

The antiserum had no cytotoxic effect on H.E.K. A neutralization titre of 1 in 80 was detected with homologous 16/60 virus, but the serum did not inhibit growth of 30/60 or H.G.P./53/60 virus.

Other Viruses

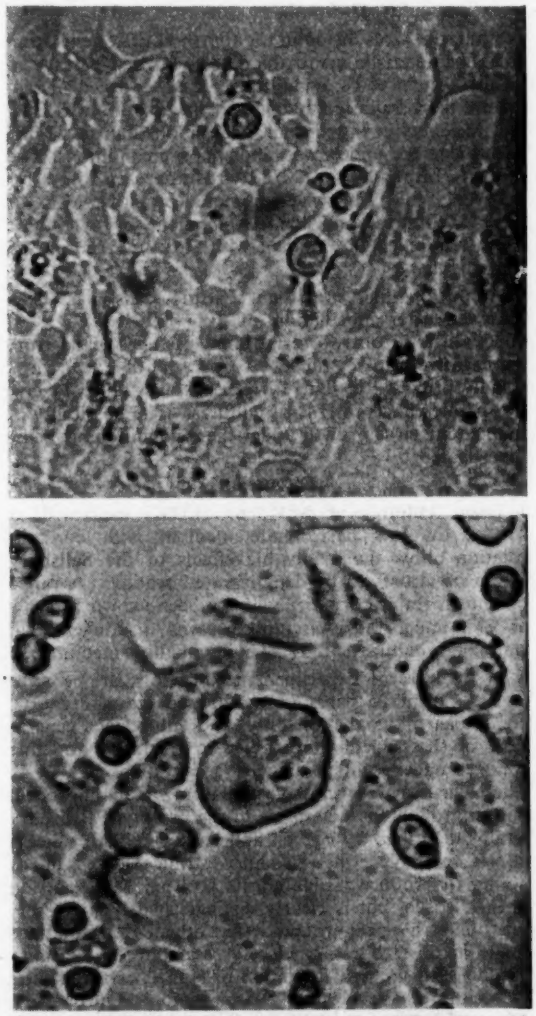
All these strains were isolated on H.E.K. only, and, though all have been passed successfully through four generations on this tissue under C.C. conditions, titres have remained low. No cytopathic change was observed after inoculation of M.K. at 33° or 37° C. or in H.E.K. at 37° C. with first to third generations of any of these strains. Preliminary neutralization spot-tests showed that in three cases (1/60, 20/60, and 119/60) antibody to the homologous virus was present at 1 in 10 dilution in the convalescent-serum sample. These sera did not neutralize 16/60 virus, but convalescent serum of Case 16/60 contained neutralizing antibody for viruses 1/60, 20/60, and 119/60.

The difficulty in obtaining supplies of H.E.K. tissue large enough for multiple neutralization-titration tests has delayed further attempts to establish the relationship of these viruses to each other, to virus 16/60, or to F.E.B., the prototype Salisbury H.E.K. virus.

Growth of Common-cold Viruses on Continued Cell Line

Fourth H.E.K. generation virus pools of H.G.P./53/60, 30/60, and 16/60 failed to produce cytopathic effects on tube cultures of M.S. or HeLa cells incubated under either C.C. conditions or routine diagnostic conditions. Further investigations are in progress to determine whether inapparent—that is, non-cytopathic—virus growth occurs in these cell lines

In tube cultures of H.EpII cells, however, inoculation of H.G.P./53/60 resulted in cytopathic changes (see Fig.) closely similar to those seen in M.K. cultures. Under routine diagnostic conditions these changes were inconstant and non-progressive, only a few small scattered foci appearing at the edges of the cell sheet. Under C.C. conditions microplaques were visible within 12 hours of inoculating 10^2 (H.E.K.) TCD_{50} of virus, and rapidly progressed to complete cell-sheet degeneration. Tissue-culture fluids harvested at 50–75% cytopathic change have undergone successful passage through four generations under C.C. conditions. The third H.EpII virus generation pool had a titre of approximately 10^5 TCD_{50}/ml. when titrated on further H.Ep.II cultures, and a 10^{-1} dilution of the pool was specifically neutralized by anti-H.G.P. antiserum. On



Cultures of H.EpII cells maintained at 33° C. in C.C. medium with 0.52% bicarbonate. Above: Normal uninoculated tube—occasional small round cells in mitosis can be seen. Below: Three days after inoculation of virus H.G.P./53/60. Large irregular refractile cells can be seen. (Unstained unfixed preparation. ×100.)

M.K. cultures this H.EpII-derived pool produced similar titres under C.C. conditions only, with typical cytopathic changes of H.G.P. virus; again growth was specifically neutralized by anti-H.G.P. antiserum.

Strain H.G.P./53/60 was successfully reisolated on H.EpII cultures from the original nasal washings after storage at −70° C. for six months.

Similarly, virus 30/60 in the fourth H.E.K. generation gave characteristic cytopathic effects on first passage to H.EpII under C.C. conditions; the harvested tissue-culture fluid produced cytopathic effects on both H.EpII and M.K. cultures under C.C. conditions, but no visible effect occurred under routine diagnostic conditions. The titre of H.EpII-derived 30/60 virus appeared to be less than 10^2 TCD_{50}/ml. when estimated on either M.K. or H.EpII cultures, and the development of cytopathic effect was much slower than with H.C.P./53/60 on the same tissue.

No cytopathic effect on H.EpII cells has been observed after inoculation of 10^3 (H.E.K.)TCD_{50} of 16/60 virus or on two serial blind passages made from the negative primary tubes. A seed pool of F.E.B. virus (kindly provided by Dr. Tyrrell) has also failed to give cytopathic effects in H.EpII cultures. The possibility of inapparent virus growth under these conditions is being investigated.

Discussion

Tissue cultures of M.K. or H.E.K. incubated at 33° C. in low bicarbonate medium with constant rotation allow the cytopathic effects of the Salisbury group of viruses to be demonstrated readily. A range of known respiratory viruses have been shown to grow as well under these circumstances as in conventional stationary cultures at 37° C. in alkaline medium.

In the present experiments eight virus strains were isolated from 25 cases of natural coryza under C.C. conditions of incubation only, and subsequent generations of these agents have failed to produce cytopathic changes under routine diagnostic conditions at 37° C. These viruses were closely similar in cytopathic effect and in growth characteristics to the prototype Salisbury strains described by Tyrrell and Parsons (1960). Strain 30/60 resembled the Salisbury strain H.G.P. in its ability to produce visible effects both on M.K. and on H.E.K. tissue, but is clearly distinguished from H.G.P. virus on serological grounds. The other seven isolations made in this laboratory closely resemble the Salisbury strain F.E.B. in their limitation to H.E.K. cultures, their cytopathic changes, and general biological properties. Virus F.E.B. was deliberately excluded from this laboratory until the present series of experiments were completed, and, as no immune anti-F.E.B. serum was available, there has yet been no opportunity of confirming the relationship of our isolates to this prototype Salisbury strain. It seems possible that the seven virus strains described may be related to each other, but they are quite distinct serologically from either the 30/60 or the H.G.P. strains which grow on M.K.-tissue culture. It is of interest that both M.K. viruses (H.G.P. and 30/60) can be propagated readily on H.EpII tissue cultures under C.C. conditions, whereas the H.E.K. viruses F.E.B. and 16/60 fail to produce cytopathic effect.

It cannot be said from these preliminary experiments that Koch's postulates are completely fulfilled, or that the agents are truly common-cold viruses. However, each of the viruses was isolated from a case with coryza only during the "cold," and nasal washings obtained after recovery were negative. No similar viruses were isolated from uninoculated-tissue-fluid passages, or from inoculations from normal individuals or cases of mild infection of the respiratory tract other than coryza. In most patients from whom a virus was isolated, neutralizing substances appeared in the convalescent serum. In two cases viruses reisolated in Salisbury from nasal washings obtained here (strains 16/60 and 30/60) have been shown in human volunteer experiments to produce an experimental coryza like that induced by H.G.P. virus (Tyrrell, personal communication).

These early results are encouraging in that they suggest that many of the findings of the Salisbury group of workers are relevant to a study of natural common colds. Further work in this laboratory will be directed to an investigation of the distribution of "cold" viruses in the general population, both by cultural and by serological means, and to the study of their aetiological role in coryza or other respiratory infections.

Summary

The effect produced by the H.G.P. strain of Salisbury viruses under low temperature and low bicarbonate conditions has been confirmed on monkey-kidney and human-embryo-kidney tissue cultures.

From 25 cases of natural coryza in Sheffield, eight virus agents with similar environmental requirements have been isolated. A rise in homologous neutralizing antibody was found in paired sera from five of the positive cases. Only one of these eight agents resembles the Salisbury H.G.P. strain in its ability to give cytopathic change on both M.K. and H.E.K. tissue culture. This virus strain, 30/60, is, however, serologically distinct from H.G.P.

Seven of the eight Sheffield isolates resembles the Salisbury strain F.E.B. in that isolation and passage were possible only on human-embryo-tissue culture. These agents are serologically distinct from the viruses capable of growth on monkey kidney, but may be serologically related to each other. Tissue cultures of the continuous cell line H.EpII support the cytopathic growth of H.G.P. and 30/60 viruses, and primary isolation has been made on this tissue. The group of viruses incapable of growth on monkey kidney failed to give cytopathic effect on H.EpII cells.

We are grateful to Miss T. Madland for assistance in the early stages of this investigation and to Dr. J. Horner for assistance in obtaining clinical specimens.

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The report on the one-day conference held on December 18, 1959, at the Royal College of Nursing on the subject of "The Employment Problems of the Home-bound Disabled" has now been published. Copies of this may be obtained from the British Council for Rehabilitation of the Disabled, price 2s. 10d. (including postage).

SERUM LEUCINE AMINOPEPTIDASE IN CARCINOMA OF PANCREAS AND OTHER DISEASES

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Leucine aminopeptidase (L.A.P.) is an enzyme which acts preferentially on peptides in which the free amino group is that of an L-leucine residue. Its presence has been demonstrated in all human tissues assayed, with high activity in the duodenum, liver, and kidney (Green, Tsou, Bressler, and Seligman, 1955; Nachlas, Crawford, and Seligman, 1957). In 1958 Goldbarg and Rutenburg described a new, simple colorimetric method for the determination of this enzyme in the serum and urine, and reported high serum levels in pregnancy and in patients with metastatic malignant disease. Later the same year, they reported their observations on leucine aminopeptidase activity in the urine and serum of patients with cancer of the pancreas and other diseases (Rutenburg, Goldbarg, and Pineda, 1958). In this paper they showed that the serum level was greatly increased in all 12 patients with carcinoma of the head of the pancreas, and that two patients with carcinoma of the tail of the pancreas had smaller but nevertheless significant increases. They also claimed that obstructive jaundice due to stones in the common bile-duct produced rises in serum activity which were smaller and less persistent than those seen in carcinoma of the pancreas, and that primary liver disease also resulted in serum elevations in general lower than those seen in pancreatic cancer.

Because of the potential clinical importance of any investigation which might facilitate the earlier diagnosis of carcinoma of the pancreas, it was decided to try to confirm these observations. During the past nine months some 500 determinations of L.A.P. levels in human serum have been carried out. It is the purpose of this paper to present the results obtained.

Method

The assay method used was essentially that of Goldbarg and Rutenburg (1958). The substrate, L-leucyl β-naphthylamide hydrochloride, is incubated with serum in a phosphate buffer solution for two hours at 37°C. At the end of this time the reaction is stopped and the proteins are precipitated by the addition of trichloracetic acid. After centrifuging, an aliquot of the supernatant is treated with sodium nitrite to accomplish diazotization of β-naphthylamine liberated by the enzyme. The addition of N-(1-naphthyl) ethylenediamine dihydrochloride then results in the development of a blue azo-dye colour which is proportional to the amount of β-naphthylamine liberated. The colour is stable for 24 hours at room temperature. The technical details of the method are given below as an appendix.

Units.—Rutenburg and Goldbarg expressed their results in terms of the Klett colorimeter reading obtained, whereas we have preferred to express ours in terms of the amount of β-naphthylamine liberated. For this purpose we have defined one unit of L.A.P. as that amount of enzyme which liberates one micromol of β-naphthylamine in two hours under the conditions of the test. We have then expressed our results as units of L.A.P. per 100 ml. serum.

The normal range was determined from a series of 107 subjects of all ages admitted to hospital without evidence of disease of the liver or biliary tract or of any other disease previously reported to give abnormal serum L.A.P. levels. For this group the mean serum L.A.P. was found to be 348 units/100 ml., with a standard deviation of 87 units. The normal range has been arbitrarily accepted as the mean ± twice the standard deviation—that is, 174-522 units/100 ml. The upper limit of normal has therefore been taken as 520 units/100 ml. While accepting that the upper limit of normal is lower for females than for males as reported by other workers, the difference has not seemed to us great enough to be of real importance in the clinical interpretation of the results obtained.

Results

Carcinoma of Pancreas

The serum L.A.P. has been studied in 16 cases of pancreatic carcinoma and the results are shown in Table I. The diagnosis was made in every case on the findings either at laparotomy or at necropsy.

TABLE I.—*Serum L.A.P. in Patients with Carcinoma of Pancreas*

No.	Site of Tumour	Bilirubin (mg./100 ml.)	Alkaline Phosphatase (K.A. Units/100 ml.)	L.A.P. (Units/100 ml.)
1	Head	12·6	38·0	2,480
2	,,	8·2	—	1,560
3	,,	16·0	—	1,245
4	,,	10·3	45·5	1,150
5	,,	10·0	76·2	1,070
6	,,	16·0	28·1	1,028
7	,,	13·9	27·1	960
8	,,	†	—	891
9	,,	12·3	35·8	680
10	,,	†	—	655
11	,,	<0·4	6·8	452
12	Neck	<0·4	—	264
13	Tail	2·4	34·2	647
14	,,	<0·4	—	496
15*	Head	<0·4	—	430
16*	,,	<0·4	16·1	870

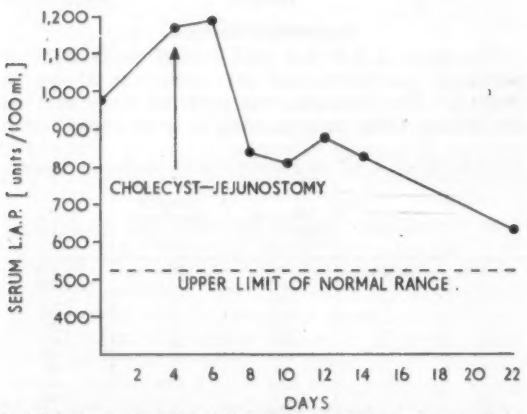
* Samples were obtained from these patients only after cholecyst-jejunostomy.
† Serum icteric bilirubin level not known.
— No contemporary determination of alkaline phosphatase done.

Three patients had tumours arising in the neck or tail of the pancreas; two of these had no jaundice, and one, with multiple hepatic metastases and malignant ascites, was slightly jaundiced (serum bilirubin 2.4 mg./100 ml.). The remaining 13 patients had carcinoma of the head of the pancreas; of these, 10 were jaundiced. In two of the three remaining cases samples were obtained only some months after cholecyst-jejunostomy for the relief of obstructive jaundice (Cases 15 and 16).

The mean serum L.A.P. level for the 14 patients on whom the determination was made before any operative procedure was carried out was 970 units/100 ml. It will be shown that this level is no greater than that commonly seen in viral hepatitis or biliary obstruction due to stones. The enzyme level was normal in the one case of carcinoma of the head of

the pancreas without jaundice and in two of the three cases of carcinoma arising in the neck or tail, although one of these patients (Case 14) had a tumour the size of a grapefruit in the tail of the pancreas. Case 15, in whom blood was obtained for the first time two months after cholecyst-jejunostomy, had an normal serum L.A.P. despite the fact that the tumour was still *in situ*, and presumably progressing, as the patient died of this disease within six months. Case 16, studied three months after a bypass operation, had a raised level, but also showed a raised serum alkaline phosphatase (16.1 K.A. units/100 ml.), suggesting possible liver metastases. The only patient (Case 13) who had a carcinoma of the tail of the pancreas and showed an increased serum L.A.P. died within a week of the determination and had multiple hepatic metastases. It will be shown that the presence of secondary deposits in the liver could explain the rise in the L.A.P. seen in these two cases.

It has been possible to follow one patient (Case 7) by serial determination after cholecyst-jejunostomy, and the results obtained are shown in the chart. The serum L.A.P. level declined rapidly after operation and had fallen to 610 units/100 ml. in 22 days, at which point the patient was discharged to convalescence.



Serial determination of L.A.P. in a patient with carcinoma of the head of the pancreas before and after cholecyst-jejunostomy. The patient was discharged from hospital on the 22nd day, and no further follow-up sample could be obtained.

From these observations it must be concluded that the elevated levels of serum L.A.P. seen in many patients with carcinoma of the pancreas are probably the result of liver damage due either to extrahepatic biliary obstruction or to the presence of hepatic metastases rather than to the pancreatic tumour itself.

Other Pancreatic Diseases

Three cases of acute pancreatitis seen all had raised levels of L.A.P., with values of 1,500, 2,010, and 820 units/100 ml. respectively. The L.A.P. was normal in one case of subacute recurrent pancreatitis in which the serum amylase was moderately raised and in two cases diagnosed clinically as having chronic pancreatitis with pancreatic insufficiency. L.A.P. was also normal in each of 10 diabetic patients examined.

Diseases of Liver and Biliary Tract

The results obtained in 53 patients are shown in Table II. In all but two cases the diagnosis given was either proved by histology, laparotomy, or necropsy, or the diagnosis was beyond reasonable doubt on clinical grounds. The two exceptions were cases of jaundice that followed operations on the cranium or face, in which there was no evidence of pre-existing liver disease and in which no wholly satisfactory diagnosis could be reached.

TABLE II.—*Serum L.A.P. Levels in 53 Cases of Liver Disease*

Diagnosis	No. of Cases	Serum L.A.P. (Units/100 ml.)
Acute hepatocellular jaundice:		
Acute necrosis of liver	1	1,740
Subacute necrosis of liver	1	1,155
Infective hepatitis	8	680; 1,330; 1,334; 985; 1,075; 1,030; 800; 892
Hepatitis complicating infectious mononucleosis	1	727
Toxic hepatitis complicating chronic urinary infection	1	825
*Post-operative jaundice ? cause	2	825; 888
Cirrhosis	12	495; 710; 1,000; 1,190; 1,070; 720; 675; 690; 392; 592; 650; 740
Intrahepatic obstruction:		
Chlorpromazine jaundice	1	1,260
Primary biliary cirrhosis	1	2,300
Extrahepatic obstruction:		
Stone in bile-duct	5	2,110; 1,070; 1,960; 1,105; 907
Inflammation of biliary tract:		
Acute cholecystitis	1	298
,, cholangitis	1	645
Chronic cholecystitis ± cholelithiasis	4	340; 296; 398; 333
Hepatic malignant disease:		
Primary malignant hepatoma (arising in cirrhotic liver)	1	737
Hepatic metastases	5	1,716; 940; 475; 1,010; 685
Vascular:		
Chronic passive venous congestion	2	705; 444
Neonatal jaundice:		
Physiological jaundice	1	655
Haemolytic disease	3	595; 550; 470
Biliary atresia	1	3,010
Familial hyperbilirubinaemia	1	298

* One case after parotidectomy, the other after operation for aneurysm of the anterior cerebral artery.

Patients with viral hepatitis in the icteric phase all showed raised serum levels of L.A.P. The mean value for the nine cases was 983 units/100 ml., which is of the same order as the mean level obtained in cases of pancreatic cancer. Values greater than 1,000 units/100 ml. were found in single cases of acute and subacute hepatic necrosis and of chlorpromazine jaundice.

The enzyme activity was increased in 10 out of 12 cases of cirrhosis examined, though the increase tended to be less than that seen in viral hepatitis, the mean value for the group being 744 units/100 ml. However, it exceeded 1,000 units/100 ml. in three cases. A marked rise was observed in a patient with primary biliary cirrhosis (2,300 units/100 ml.), and this observation has been confirmed on several occasions.

In five patients with cholelithiasis and obstructive jaundice the mean level was found to be 1,430 units, which is higher than the mean for all cases of carcinoma of the pancreas.

A patient with a malignant hepatoma arising in a cirrhotic liver showed a moderate increase (737 units), and a raised L.A.P. was found in four of five patients with proved hepatic metastases.

The patients examined with acute or chronic cholecystitis with or without cholelithiasis showed normal levels.

A baby with congenital biliary atresia showed the highest level seen in this series (3,010 units). The levels in four other neonates examined with physiological jaundice or jaundice due to haemolytic disease were only slightly above the normal adult limits and in no case exceeded 700 units.

Malignant Disease

The results obtained in 20 cases of proved malignant disease, other than carcinoma of the pancreas, are shown in Table III. Seven patients showed elevated levels of L.A.P. Of these, four had proved liver metastases, one had a carcinoma of the ampulla of Vater with obstructive jaundice, and the other two had minimal rises only (572 and 545) and could possibly have had undetected liver secondaries. The case of carcinoma of the ampulla of Vater is of considerable interest, in that this patient presented with a clinical picture and operative findings indistinguishable from carcinoma of the head of the pancreas. The L.A.P. was greatly increased and fell rapidly after cholcyst-jejunostomy, regaining the normal level within three weeks. This case again emphasizes that biliary obstruction produces a rise in L.A.P., and that this rise is independent of the nature of the pathology producing the obstruction.

TABLE III.—*Serum L.A.P. in 20 Cases of Carcinoma Other than Carcinoma of Pancreas*

No.	Site of Tumour	Proved Hepatic Metastases	Serum L.A.P. (Units/100 ml.)
1	Breast	−	572
2	,,	−	276
3	,,	−	354
4	,,	−	472
5	Bronchus	−	427
6	Pharynx	−	287
7	Oesophagus	−	545
8	Stomach	−	246
9	,,	−	420
10	Ampulla of Vater	−	1,290
11	Colon	−	320
12	Sigmoid	−	464
13	Kidney	−	417
14	Bladder	−	286
15	,,	−	417
16	Breast	+	1,716
17	Bronchus	+	940
18	Caecum	+	475
19	Colon	+	1,010
20	Rectum	+	685

+ Indicates proved hepatic metastases noted either at operation or at necropsy.

The remaining cases all had L.A.P. levels within the normal range.

Miscellaneous Disease

The serum L.A.P. has been determined in a wide range of miscellaneous conditions, but no significant abnormalities have been found. In particular it is perhaps worth recording that it is normal in most cases of myocardial infarction, though in patients who are in failure or are profoundly shocked there is sometimes a small rise possibly due to anoxaemic liver-cell damage. Renal failure with uraemia does not result in retention of the enzyme with elevated serum levels. Normal levels have been demonstrated in the reticuloses and collagen diseases without evidence of hepatic involvement.

Discussion

These findings are in agreement with those of Arst, Manning, and Delp (1959), who state that normal L.A.P. levels are found in a wide variety of malignant, neurological, cardiovascular, haematological, gastro-intestinal, renal, dermatological, and infective disorders, but that almost any condition which affects the liver may produce abnormal serum levels of the enzyme.

We have been unable to confirm the clinical usefulness of this determination for the diagnosis of carcinoma of the pancreas. The increases seen in this condition are no higher than those seen in viral hepatitis or in jaundice due to intrahepatic or extrahepatic obstruction from other causes. Moreover, three cases reported here, which were not jaundiced and had no evidence of hepatic metastases, had normal L.A.P. levels—despite the fact that one patient with a carcinoma of the tail of the pancreas had a tumour the size of a grapefruit. After bypass operations for the relief of obstructive jaundice produced by pancreatic cancer, the L.A.P. can be shown to fall, although the tumour is still *in situ*. It must be concluded than any rise in serum L.A.P. which occurrs in patients with pancreatic carcinoma is in no way directly related to the presence of the neoplasm.

The determination has little promise as an aid to the differential diagnosis of jaundice, since it is less effective than the commonly available tests in differentiating between jaundice due to extrahepatic obstruction and that due to hepatocellular disease.

The finding of a very high level in a baby with congenital biliary atresia does suggest a possible limited usefulness in clinical medicine. The diagnosis of extrahepatic obstruction in the neonatal period is notoriously difficult; the van den Bergh reaction is often negative owing to inefficient conjugation of bilirubin with glucuronic acid by the liver, and urobilinogen is normally absent from the urine in neonates owing to the absence of a bacterial flora in the gut. A test which could reliably detect obstruction might be of considerable value.

It has not been possible as yet to establish the normal neonatal range for serum L.A.P., but it seems unlikely that the high level found in the maternal serum in the last trimester of pregnancy crosses the placental barrier; and the upper limit of normal in babies is probably not much greater than that for adults. Results so far suggest only minor elevations of L.A.P. in physiological jaundice and jaundice due to Rh—or ABO-incompatibility. Possibly consideration of the L.A.P. level in conjunction with the isocitric dehydrogenase value (which in adults is normal in extrahepatic obstruction, but much raised in liver-cell necrosis) may permit earlier and more certain recognition of congenital biliary obstruction. It is, however, clear that much further work will be required before any conclusive evidence can be submitted on this point.

Summary

Serum leucine aminopeptidase (L.A.P.) may be determined for clinical purposes using L-leucyl β-naphthylamide hydrochloride as the substrate. The method is simple and satisfactory.

Raised serum levels are seen in pregnancy, acute pancreatitis, viral hepatitis, necrosis of the liver, chlorpromazine jaundice, liver metastases, extrahepatic biliary obstruction, and in some cases of cirrhosis.

There is no evidence that the determination is of any value as an aid to the diagnosis of carcinoma of the pancreas.

APPENDIX

Estimation of Leucine Aminopeptidase

Reagents

(1) L-leucyl β-naphthylamide hydrochloride solution, 0.4 mg./ml.

(2) 0.2 M phosphate buffer, *p*H 7; 0.2 M Na_2HPO_4, 6.1 parts; 0.2 M KH_2PO_4, 3.9 parts.

Equal volumes of reagents 1 and 2 are mixed to yield a substrate-buffer solution, *p*H 7.1, stable at room temperature for 30 days.

(3) Trichloracetic acid solution, 12%.

(4) Trichloracetic acid solution, 40%.

(5) Sodium nitrite solution, 0.1%.

(6) Sodium sulphamate solution, 0.5%.

(7) N-(1-naphthyl) ethylenediamine dihydrochloride solution, 0.5 mg./ml. in 95% ethanol.

Method

1 ml. of a 1:50 (2%) dilution of serum in distilled water is added to 1 ml. of the substrate-buffer solution. A control is prepared by adding 1 ml. of distilled water to 1 ml. of substrate-buffer solution. The test and control are both incubated at 37° C. for two hours.

At the end of this time the reaction is stopped and the proteins are precipitated by the addition of 1 ml. of 12% trichloracetic acid. After centrifuging, a 1-ml. aliquot of the supernatant is pipetted off and 0.2 ml. of 40% trichloracetic acid is added, and mixed by gentle shaking. (The original method described for protein precipitation was found to be unsatisfactory in that it sometimes resulted in turbidity in the final solutions.)

1 ml. of 0.1% sodium nitrite solution is added. Leave for five minutes. Any excess nitrite is then destroyed by the addition of 0.8 ml. of 0.5% sodium sulphamate solution. This reaction is complete in three minutes.

2 ml. of N-(1-naphthyl) ethylenediamine dihydrochloride solution is then added. The maximum blue colour develops in 15 minutes, and after this the optical density (O.D.) is read against the control at 580 mμ.

The colour is stable for 24 hours at room temperature.

The O.D. reading is converted to terms of β-naphthylamine liberated by reference to a standard calibration curve prepared with β-naphthylamine. When an O.D. greater than 0.700 is obtained, the procedure is repeated using an incubation time of one hour only, and the result obtained is doubled.

Our thanks are due to Miss Johnson, of the Edgware General Hospital, Dr. H. Caplin, of the Connaught Hospital, and Dr. P. Mestitz, of the Middlesex Hospital, all of whom supplied sera from patients with carcinoma of the pancreas. Also to Mr. Cowan, records officer, Middlesex Hospital, and his staff, who helped us with the follow-up of patients examined; and to the staff of the Bland-Sutton Institute, who provided access to histology and necropsy reports. Mr. M. Thomas and Mr. H. Stevens gave valuable help in overcoming initial technical difficulties. Finally, we should like to thank Professor Sir Charles Dodds for his advice and encouragement.

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A World Health Organization Expert Committee on Mental Health, which has just ended a session in Geneva, decided that research on an international as well as a national scale is necessary if further advances are to be made in preventing mental illness. The Committee defined areas of priority for mental health research, placing high on the list researches into brain function, social attitudes, effect of cultural change, psychoses of the aged, effects of nutrition, and genetic factors. In its opinion the administration of mental health programmes should also be studied. (W.H.O./59.)

PSYCHOGENIC URINARY RETENTION AFTER PARTURITION, RESULTING IN HYDRONEPHROSIS

BY

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Urinary retention in women may occur in association with a wide variety of disorders such as retroverted gravid uterus, haematocolpos, uterine fibroids, and ovarian or broad-ligament tumours. Occasionally it is the presenting symptom in multiple sclerosis. Again, it is a common feature of the immediate post-partum period when bladder tone is reduced and large quantities of retained urine can be tolerated without producing a strong desire to micturate. Bruising and oedema of the bladder neck, perineal lacerations, and sutures are also contributory factors, but normal micturition is usually re-established within a few days.

Nevertheless, in a substantial proportion of cases no organic cause can be found to explain the disturbance. Emmett, Hutchins, and McDonald (1950) studied 76 cases of urinary retention in women who had attended the Mayo Clinic, and in the majority were unable to demonstrate a definite causative factor. They examined microscopically tissue removed from the vesical neck during transurethral resection in each of these cases, and noted that fibrosis, inflammatory reaction, and glandular hyperplasia were not significant factors in the production of obstruction. They advocated transurethral resection of the bladder neck as the treatment of choice, and 81% of their patients had a favourable response.

In such cases where there is an incomplete understanding of the underlying mechanism in physical terms psychiatric evaluation would seem to be indicated. Many standard medical and surgical reference books comment briefly that urinary retention may occur as a hysterical symptom which usually responds to reassurance, although occasionally catheterization may be required. However, so far as can be ascertained there have been only two relevant psychiatric studies reported in the literature. Williams and Johnston (1956) demonstrated the primary importance of emotional factors in a 28-year-old woman suffering from recurrent retention. Psychotherapy resulted in elimination of the symptom. Chapman (1959) described a further case where the patient's symptom was related to sexual trauma, seduction, and rape by her stepfather. Psychotherapy was directed towards exploration of her hostility towards this relative, and it was noted that her episodes of retention occurred when her hostility threatened to become conscious. Again, psychotherapy led to the disappearance of the symptom.

This presentation outlines the psychological aspects of a further case where retention was on a hysterical basis. The term "hysteria" is employed here to denote a psychogenic condition where the symptoms presented by the patient are not motivated in full consciousness and are employed for the sake of some gain. Such an illness usually does not progress to the development of irreversible damage, although this may occasionally occur when protracted hysterical paralysis of a limb leads to muscular contractures. However, it must be almost unique for the patient to persist with a symptom

to such an extreme as to endanger life by the production of irreversible pathological change in a vital organ.

This case may be of interest in view of the paucity of similar studies in the literature, and particularly as psychogenic urinary retention resulted in a severe degree of renal impairment. Again, it may suggest that intractable cases of urinary retention, in the absence of any demonstrable organic cause, warrant psychiatric assessment before surgical procedures are embarked upon. However, as William and Johnston were careful to point out, "only research in a number of cases will justify the conclusion that emotional factors often can be of primary specific significance in the aetiology of cases heretofore baffling."

Case History

The patient, a 25-year-old housewife, had a forceps delivery on June 1, 1959, for delay in the second stage of labour, and gave birth to a living male child weighing 7 lb. (3,175 g.). Some hours later she was cautioned by a nurse that for a few days she might have some difficulty in micturition, and this proved to be the case. She was catheterized for several days and discharged home on the eighth day, although it is uncertain whether normal micturition had been re-established by this time.

She was readmitted two weeks later complaining of crampy lower abdominal pain, and was found to have a distended bladder containing 52 oz. (148 ml.) of urine. During the next few weeks she could pass only small amounts of urine, and was treated with periods of intermittent or continuous catheterization. It was postulated that the bladder had been damaged during delivery, and it was expected that tone would gradually be regained. Carbachol produced evacuation on one occasion, but was subsequently avoided as it made her nauseated and feel faint. Her physical condition deteriorated, she lost weight, and developed a normochromic normocytic anaemia and urinary infection. As cystoscopy produced negative findings she was transferred to a general hospital eight weeks later, with a view to investigating the possibility of an underlying neurological disorder.

No abnormal signs were noted on routine examination of the central nervous system, and *x*-ray examination showed that the chest and lumbar spine were normal. A lumbar myelogram was performed and the contrast medium passed normally from the lumbar to the cervical region, through the foramen magnum, and into the anterior basal cisterns, there being no evidence of any abnormality. Examination of the cerebrospinal fluid gave normal readings. Again, in view of her anaemia, which was not responding satisfactorily to oral iron preparations, a sample of marrow was aspirated from the sternum. This showed an active granulopoiesis with hypoplastic erythropoiesis. An intravenous pyelogram was performed on September 1. The right kidney showed poor excretion of the contrast medium and the upper calices were poorly defined, showing some dilatation. It was difficult to identify the middle and lower calices, but there appeared to be some contrast medium present in these. The left kidney showed a gross hydronephrosis and hydroureter, and the contrast medium had passed into the bladder, which appeared to be rather large. It was concluded that the appearances were consistent with a bilateral hydronephrosis probably due to an obstruction in the bladder.

The patient continued to have retention of urine, requiring continuous catheterization, and on September 10 she had a suprapubic cystotomy. By this time there was a gross anaemia and emaciation was marked; her blood urea was 129 mg./100 ml. and she was acidotic, with a CO_2-combining power of 17 mEq/litre. She was treated with appropriate electrolyte correction and had a good urinary output from the suprapubic tube. The urinary infection was treated initially with neomycin and then with "distaquaine G" and nitrofurantoin. The blood urea fell over the next few days to 47 mg./100 ml. after a diuresis. However, urinary infection continued to be troublesome, and an almost continuous pyrexia persisted until October 2. During this period the blood urea fluctuated between 60 and 80 mg./100 ml., and supplements of sodium bicarbonate and potassium chloride were required. By October 9 pyrexia had recurred and the urine contained *Proteus* or coliforms from time to time, but always numerous pus cells. Within five days the patient was afebrile, having had chloramphenicol, but pyrexia recurred as soon as this was discontinued.

The suprapubic catheter was removed on October 12; a self-retaining catheter was inserted, released two-hourly, and a good urinary output was maintained. On October 16 the catheter was removed and she was able to pass 10 oz. (284 ml.) of urine, but the suprapubic wound continued to drain urine and a Foley catheter was inserted. On November 5 the bladder was explored surgically and the vesical neck appeared normal. The suprapubic fistula was closed, but further episodes of retention occurred when the self-retaining catheter was removed; blood urea rose to 100 mg./100 ml. and intermittent pyrexia developed. A low-protein diet, electrolyte correction, and fluid-balance management were required. Two weeks later it was possible to put her back on a normal diet, and she was given 3 pints (1.7 litres) of packed cells. Again her pyrexia subsided with chloramphenicol, but it recurred again as soon as this was withdrawn. The coliform organisms had become resistant to all antibiotics other than kanamycin and neomycin, and after a course of kanamycin she was apyrexial.

Psychiatric Evaluation

At this point the patient was referred for psychiatric evaluation, and was transferred to this department on December 1.

On admission she was grossly emaciated, weighing 5 st. 6½ lb. (34.7 kg.), her weight prior to the pregnancy being approximately 7 st. 5½ lb. (47 kg.). There were no other abnormal signs on physical examination, and particularly no hypertension or retinal changes. Blood urea was 46 mg./100 ml., and the self-retaining catheter was still required.

Detailed exploration of the psychogenic factors which seemed to be operating produced the following information.

The patient was an only child, and she described her father as an irritable and quick-tempered alcoholic who, when intoxicated, became violent, and on several occasions had injured his wife quite severely. He gave his family little financial support, and before entering her teens the patient was sewing and knitting for neighbours in order to earn enough to clothe and maintain herself at school. She could recall only a few isolated incidents when he showed a modicum of kindness, and her predominant recollections were of "brutality and fear." In contrast, the patient described her mother as a kindly and industrious person who, for many years, had tolerated her husband's behaviour, trying to excuse his conduct to the child. The patient would seem to have been rather dependent on her mother, and discussed how from childhood she has always dreaded their parting by death.

Three years ago her parents were legally separated, and about this time—that is, at the age of 20—the patient was married. Her mother has continued to live with her. She spontaneously suggested that her father's behaviour may have had a considerable part to play in the development of her sexual attitudes. The attitude which was evident in his relationship to the family group was extended in fantasy by the patient to involve his sexual relations with her mother. This was to the patient another form of assault in which her mother was an unwilling and helpless partner. This impression had not been corrected by any education, and information was accumulated from girls of her own age. In this setting sexual relations "became horrible and disgusting to me; I always knew it was something I couldn't do—it was the type of thing I would never ask anyone to

do." In spite of her parents' separation, her fantasies with regard to her father persisted. Thus she dreaded arriving home after being away for a few hours lest her father had returned in the interval and severely injured her mother.

Prior to the patient's own marriage she discussed their future sexual relationship with her husband, and claimed that they had reached a mutual agreement whereby intercourse would not occur until they decided to have a family. Accordingly, it took place for the first time about 18 months after marriage, and again one month later, when the patient became pregnant, after which it was avoided. On both occasions sexual intercourse was painful, unpleasant, and repugnant. Throughout pregnancy she remained well, and vomiting was not a problem. When further exploration of her sexual attitudes and fantasies was attempted she became, and remained, extremely reticent and evasive. In an attempt to verify her statements and expand the account available, her husband was interviewed by another member of the medical staff. He also was uncommunicative, but agreed that intercourse had occurred on only two occasions. He denied that his sexual relationship with his wife constituted a problem.

The patient's attitude to the child was explored, and there was evidence of rejection as expressed through compensatory overprotection, and this has been confirmed since her discharge from hospital. It has taken the conscious form in such ways as a fear that the child may become ill or that it may drown in its bath, and by being excessively cautious lest she should drop it.

After 10 days in hospital, and of her own volition, she agreed to having the catheter removed, and from then until her discharge four weeks later her urinary output remained quite satisfactory, and at no time was there any evidence of retention of urine. She felt she could micturate with normal force, and never complained of bladder discomfort. In spite of this dramatic improvement she did not appear to gain an understanding of the true nature of her symptom, although accepting that it was not primarily on a physical basis. She remained quite inflexible in her attitude to further intercourse, even scorning advice regarding contraceptive techniques, holding that she had been advised by various doctors that, in view of the consequences of her first pregnancy, it would be inadvisable to have a further child. It then transpired that, coinciding with her improvement, she had secured her husband's agreement to have no further intercourse.

Physical Treatment

In association with psychotherapy, physical treatment was obviously indicated, and may here be outlined. In view of the considerable weight loss she had a three-weeks course in modified insulin therapy which was instituted and maintained cautiously in view of her very debilitated state. The maximum dose given was 10 units, and this, in combination with norethandrolone, resulted in an increase in weight of 22 lb. (10 kg.). Ferrous succinate did not produce any marked increase in her haemoglobin level, which was 69% on admission and 71% on discharge. She remained apyrexial, but pus cells persisted in her urine, and on several occasions *Proteus vulgaris* was cultured. The pyuria was unresponsive to antibiotics. Her electrolyte status remained satisfactory throughout her stay, and she did not require supplements. As normal micturition was re-established her blood urea fell and was maintained between 34 and 40 mg./100 ml. during the three weeks prior to her discharge, and menstruation occurred for the first time since the pregnancy.

Before she left hospital her renal function was assessed in order to determine the degree of impairment at that time and to establish a baseline for comparison in the future. (1) Glomerular filtration rate, 50 ml. a minute. (2) Specific gravity range test: there was a maximum concentration of 1015 and a minimum specific gravity of 1002. In addition, serum protein electrophoresis showed a total protein of 7.2 g./100 ml. The pattern showed a normal albumin level but a slight reduction in the globulin fraction. Total urinary protein was 0.28 g. in 24 hours.

Discussion

The initial formulation of the retention was that the symptom had meaning to the patient as the result of an injury in childbirth. Her choice of symptom may have been determined by a transient retention due to local trauma during labour or iatrogenically produced by a nurse's chance remark ; probably both factors were operating. The retention came to represent the patient's protest against pregnancy and motherhood, and insurance against further intercourse and its consequences. Exclusively physical methods of treatment employed initially had perhaps reinforced her belief that the symptom had a physical explanation.

The psychiatric approach served to widen this belief, and in a series of interviews her sexual development from childhood to marriage was focused upon, while at the same time it was tacitly accepted that the catheter would be removed when she felt she could pass urine normally. An implicit understanding was built up between the patient and the therapist that her real problem was being attended to, and it was in this setting that she tolerated removal of the catheter while at the same time securing her husband's agreement that further intercourse would not occur.

The glomerular filtration rate demonstrated that the functional capacity of the kidneys had been reduced to less than 50% of normal, and there was evidence that a chronic pyelonephritis had developed. As such infection is notoriously difficult to eradicate, even when the underlying mechanical obstruction has been relieved, the prognosis from the physical standpoint must be guarded, and progress to chronic uraemia may occur. Specialist supervision of this problem was indicated, and has been undertaken.

The unsatisfactory adjustment made by the patient to her problems would not have been regarded as adequate in a case where retention was uncomplicated by renal damage. To have produced a completely satisfactory sexual adjustment in this instance did not seem to be such a desirable therapeutic goal as usual, in the light of the physical considerations. Of course, whether it would have been possible to bring about such an adjustment is open to doubt. The risk of more intensive psychotherapy was that instead of producing an abolition of retention, as was achieved, the patient may again have retreated to her symptom with further rapid deterioration in renal function.

Summary

A case of urinary retention in a young woman in whom emotional factors were found to be of primary importance is outlined, and the psychodynamics are discussed. When the patient arrived at an adjustment to her problems the symptom was eliminated. However, by then a severe degree of renal impairment had occurred and bilateral hydronephrosis had been established.

I am indebted to Professor J. G. Gibson, department of mental health, Queen's University, for permission to report this case, and for advice in the preparation of the paper. My thanks are also due to Dr. M. McGeown, department of medicine, Queen's University, for supervising the medical treatment.

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MENSTRUATION AND ACCIDENTS

BY

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Whitehead (1934) observed that in some air accidents involving women air pilots, in which the cause of the accident could not be found, the pilots were in the menstrual phase of the cycle. Although there have been many studies in other fields of accident proneness, little attention appears to have been given to the part played by menstruation. During work on the diseases of menstruation it was observed that premenstrual lethargy and irritability result in a slow reaction time and loss of judgment. As both judgment and reaction time are important factors in the avoidance of accidents, it was felt that a study of women involved in accidents might reveal a correlation between the accident and menstruation.

The survey was carried out in four London general hospitals where accident wards were visited once or twice a week. Women admitted as a result of an accident and between 15 and 55 years were interviewed by me. Women in my practice who had been in an accident requiring immediate medical attention were also included. Patients in hospital considered by the sister to be too ill for an interview, those who could not speak English, and those who were deaf were excluded. In addition to ascertaining their age, parity, and marital state, the patients were asked how the accident occurred, whether they had previously been involved in an accident, their previous state of health, the duration of menstruation, the length of their menstrual cycle, and, finally, the date of their last menstruation.

Results

Of a total of 124 women involved in accidents, 84 had menstruated during the 28 days prior to the accident. The reasons for amenorrhoea in the remaining 40 women are shown in Table I.

Among the women who were menopausal there appears to be an unduly high proportion (34.6%) who had an artificially induced menopause. All nine women had undergone a hysterectomy, with or without an oophorectomy.

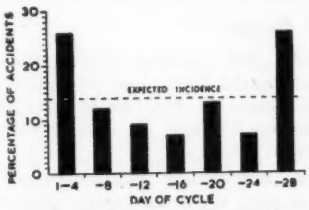

FIG. 1.—Distribution of 84 accidents in the menstrual cycle.

The menstrual cycle of 28 days was divided into seven four-day periods, in which Days 1–4 represented menstruation, Days 13–16 ovulation, and Days 25–28 premenstruum. The time in the menstrual cycle at which the 84 regularly menstruating women were involved in an accident is shown in Fig. 1. More than half of all these accidents occurred during menstruation or the four days preceding menstruation. The probability of such a distribution occurring by chance is less than one in a thousand ($\chi^2 = 23.3$ on 1 d.f.), and therefore indicates that menstruation is a significant factor in accident-proneness.

TABLE I.—*Reasons for Amenorrhoea in 40 Women*

Previous menstruation 29–42 days (possibly early pregnancy)	5
Puberty	2
Pregnancy	2
Puerperium	2
Natural menopause	17
Artificial ,,	9
Unable to recall date of last menses	3

TABLE II.—*Distribution of Accidents During the Premenstruum and Menstruation*

Type of Accident	During Premenstruum and Menstruation. Patients	Total No. of Patients	χ^2 on 1 d.f.	Probability
All accidents	44 (52%)	84	23·3	0·001
Major hospital	18 (49%)	37	7·3	0·01
Minor ,,	18 (60%)	30	14·6	0·001
General practice	8 (47%)	17	2·9	0·1
Active participant	35 (52%)	66	19·4	0·001
Passive ,,	9 (50%)	18	4·0	0·05
Home	14 (64%)	22	13·3	0·001
Road	23 (49%)	47	9·7	0·01
Habitual actions	18 (51%)	35	9·0	0·01

Table II shows a further analysis of these 84 women, giving the number of women involved in different types of accidents during menstruation and the premenstruum, compared with the total for each group. The definitions used were:

Major accidents involving a fracture or loss of consciousness exceeding one hour.

Habitual actions covered accidents occurring during the performance of routine everyday work—for example, walking down stairs, factory work.

Active participation occurred where greater judgment on the part of the injured might possibly have lessened the severity of the accident—for example, driver of a vehicle.

Passive participation occurred where some other person was wholly responsible for the accident, and greater judgment on the part of the injured would have been of no avail in preventing the accident—for example, passenger in a vehicle.

With a purely random distribution of accidents, two-sevenths (28.5%) of the accidents of any one type would be expected to fall within the four-day periods of menstruation and premenstruum. In fact, Table II shows that the percentage of accidents occurring within these eight days is much higher. The significance of this preponderance is shown by the chi-square test, on one degree of freedom; and for all types, except accidents in general practice (the numbers of which were very small), the probabilities are very low. These results are therefore highly significant.

The fact that a significantly high proportion of both active and passive participants were involved in accidents during menstruation and the premenstruum suggests that it is not only judgment which is of importance.

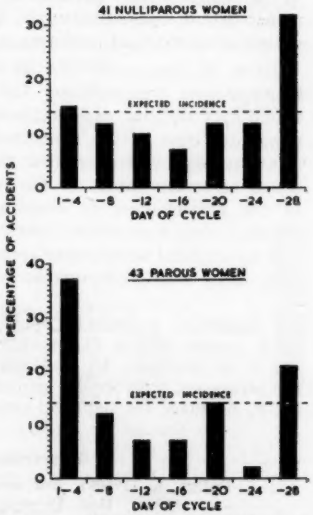

FIG. 2.—Distribution of accidents in nulliparous and parous women.

There is an unexpected difference in the distribution of accidents in the nulliparous and parous women (Fig. 2); for in the nulliparous women the accidents occur predominantly during the premenstruum, while in the parous women a high incidence occurs during both the premenstruum and the menstruation. This difference is not associated with marital state, for married women with no children tended to be more accident-prone during the premenstruum. Nor was there any tendency for the time of accident-proneness to differ among the women with one child from the women with many children. It may be that, whereas the nulliparous woman tends to have a heavy menstrual loss from the first day, the parous woman often has a slight loss for one to three days before the full menstrual flow begins. If lethargy of the premenstruum is due to water retention, which is relieved by the full menstrual flow, then one would not expect all parous women to be relieved of their lethargy until the fourth day of menstruation.

Only 13 women had previously been involved in an accident, and these were evenly scattered among the seven four-day periods. Sixty-two women described their previous health as "good," 15 as "moderate," and 7 as "poor," and these also were evenly distributed throughout the cycle.

Conclusions

In this survey 44 (52%) of a total of 84 regularly menstruating women were involved in an accident during menstruation or the four days before menstruation. The significance of menstruation as a factor affecting accident-proneness persisted among home, road, and factory accidents, while women were performing routine actions, and among the active and passive participants of an accident. It is suggested that the increased lethargy of menstruation and the premenstruum is responsible for both a lowered judgment and slow reaction time. Schoolgirls' work deteriorates during menstruation (Dalton, 1960a), and they are more likely to be punished for unpunctuality and forgetfulness during menstruation (Dalton, 1960b). Wickham (1958) found that the intelligence-test scores in women Army personnel were lowered during menstruation, but, surprisingly, this did not hold for the practical/mechanical performance test.

These findings cause one to consider the wisdom of administering tranquillizers for premenstrual tension, which may well increase accident-proneness at the most dangerous time of the menstrual cycle. One wonders if awareness by women that they are more accident-prone at certain times of the month will enable them to use greater care in avoiding accidents, or will it merely induce a menstrual neurosis? Women who have had an artificial menopause appear more accident-prone than those whose menopause was natural.

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IRON-DEFICIENCY ANAEMIA IN EUROPEAN AND WEST INDIAN INFANTS IN LONDON

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The high incidence of anaemia in West Indian infants which was found during a study of atopic eczema (Marten, Sarkany, and Davis, 1960) led to the present investigation. Anaemia due to dietary deficiency, intestinal worms, or a combination of the two is common in negro children living under tropical conditions (Wolman, 1957). Munday *et al.* (1938) studied the haemoglobin levels of negro and white infants living under similar conditions in a non-tropical area. They showed that from the age of 4 months onwards negro infants in the United States had lower haemoglobin levels.

The present study compares the haemoglobin levels of West Indian and European infants suffering from eczema with healthy control groups. The West Indian infants were all born in this country and had never lived abroad. The healthy infants, drawn from local day nurseries, had no history of eczema and had no known illness at the time of examination.

Methods.—The haemoglobin level and packed cell volume were measured on capillary blood using Haldane's technique (100% = 14.8 g./100 ml.) and micro-haematocrits. From these the mean corpuscular haemoglobin concentration (M.C.H.C.) was calculated. All the West Indian infants were tested for sickling, and "cellophane" swabs and stools were examined for ova. Eczematous infants with haemoglobin levels below 70% (10.3 g./100 ml.) were treated with oral iron (elixir of ferrous gluconate).

Results

Excluding four infants with positive sickling tests, 114 infants, whose ages ranged from 5 to 23 months, were investigated. Of these, 54 had atopic eczema (West Indian 21, European 33) and 60 were healthy (West Indian 26, European 34).

The infants in these four groups had comparable birth weights and age ranges, while the healthy infants had similar weights at the time of examination. With Fisher's "t" test no statistically significant difference between the means of these values could be demonstrated (Table I).

Statistical comparisons of the mean haemoglobin levels and the mean M.C.H.C.s for both West Indian and European groups have been made, and the results are shown in Table II. It will be seen that for each race there was no significant difference between the eczematous and healthy groups. However, when the two races were compared the mean haemoglobin levels

TABLE I

Groups Studied	No. of Infants	Age (Months) Mean±S.D.	Age (Months) Range	Birth Weight (oz.) Mean±S.D.	Birth Weight (oz.) Range	Present Weight (oz.) Mean±S.D.	Present Weight (oz.) Range
West Indian A. With eczema	21	12·8±5·5	5–22	111·5±12·8	70–146	—	—
West Indian B. Healthy	26	13·4±5·3	5–22	111·4±15·2	83–136	349·2±74·9	199–508
European C. With eczema	33	12·9±5·2	5–23	115·1±15·1	89–150	—	—
European D. Healthy	34	13·4±4·9	5–23	115·7±17·2	89–145	347·8±63·7	288–473
Comparing Groups	**n**	**t**	**p**	**t**	**p**	**t**	**p**
A and B	45	0·358	0·7	0·033	>0·9	—	—
A ,, C	52	0·028	>0·9	0·882	0·2	—	—
A ,, D	53	0·374	0·7	0·930	0·2	—	—
B ,, D	58	0·024	>0·9	0·980	0·2	0·077	>0·9
B ,, C	57	0·331	0·7	0·920	0·2	—	—
C ,, D	65	0·401	0·6	0·139	0·8	—	—

TABLE II

Group*	No. of Infants	Haemoglobin (%) (g./100 ml.) Mean±S.D.	Haemoglobin (%) (g./100 ml.) Range	M.C.H.C. (%) Mean±S.D.	M.C.H.C. (%) Range
A	21	60·9±8·9 (9·0±1·3)	48–86 (7·1–12·7)	27·6±1·0	21–34
B	26	62·3±10·0 (9·2±1·5)	40–78 (5·9–11·5)	29·0±2·8	22–33
C	33	73·8±6·8 (10·9±1·0)	54–80 (8·0–11·8)	30·6±2·0	25–35
D	34	72·1±6·1 (10·6±0·9)	58–84 (8·6–12·4)	31·4±1·9	27–35
Comparing Groups	**n**	**t**	**p**	**t**	**p**
A and B	45	0·64	0·5	1·47	0·1
A ,, C	52	5·89	<0·001	4·07	<0·001
A ,, D	53	5·40	<0·001	5·23	<0·001
B ,, C	57	4·53	<0·001	2·63	0·02
B ,, D	58	4·41	<0·001	3·90	<0·001
C ,, D	65	1·06	0·2	1·47	0·1

*See Table I for particulars of grouping.

and M.C.H.C.s were significantly lower in the West Indian infants.

Thus it appeared that the West Indian infants with atopic eczema had lower haemoglobin levels than their European counterparts, but since similar results were obtained in the healthy groups these findings were considered incidental and unrelated to the atopic eczema.

In order to determine whether the differences in haemoglobin levels occurred throughout the age range of 5 to 23 months the infants were divided into three-monthly age-groups. As the findings in the eczematous and healthy infants of each race were similar they have been combined (Fig. 1).

The West Indian infants had lower means, and, with one exception, lower ranges in each three-months period. In each race there was a fall in the mean levels up to the age of 1 year, followed by a rise, which was perhaps slower in the West Indians. The maximum difference between the means (14.4%, or 2.1 g./100 ml.) was found in the 17 to 19 months age-group.

The lower mean M.C.H.C.s as well as the lower mean haemoglobin levels in the West Indians indicated a higher incidence of iron deficiency. An indication of the incidence of iron deficiency was obtained by excluding children with normal M.C.H.C.s. For this purpose 30% was taken as the lower limit of normal, as in our experience values as low as 30% have been found in children whose haemoglobin levels were well within the adult range. Among the West Indian infants 53.5% (25/47) had M.C.H.C.s below 30%, compared with 22.4% (15/67) of the European infants.

Comparison of the haemoglobin levels in the children with M.C.H.C.s of 30–34%—that is, normal values—showed that in each three-months group the West Indians had lower means, and, in most cases, lower ranges (Fig. 2). This suggested that there was a racial difference between the normal ranges at this age. The lowest means were reached in the 11 to 13 months group, and were 73% (10.8 g./100 ml.) for the Europeans and 62% (9.2 g./100 ml.) for the West Indians.

No ova were found in any of the cellophane swabs or faeces.

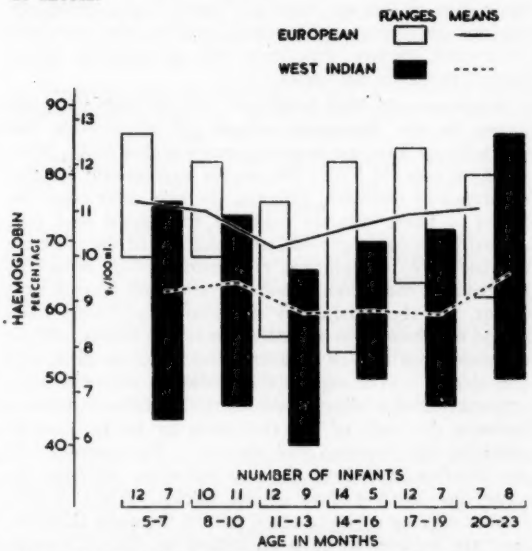

FIG. 1.—Comparison of haemoglobin levels in West Indian and European infants.

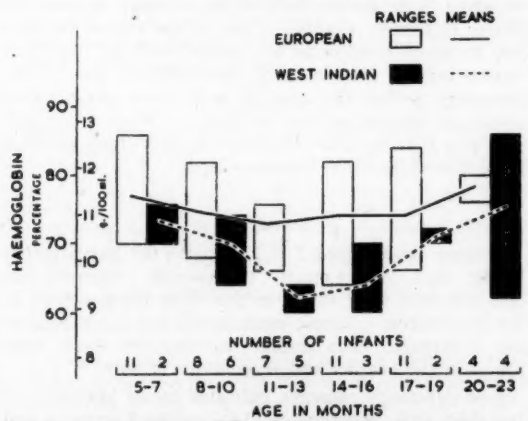

FIG. 2.—Comparison of haemoglobin levels in West Indian and European infants with M.C.H.C.s of 30–34%.

Anaemia in the eczematous infants was treated with oral iron for 8 to 12 weeks, and a satisfactory response occurred in all cases of both races.

Discussion

Our results show several important differences between the West Indian and European infants. It appears that there may be an intrinsic racial difference between the mean haemoglobin levels of healthy negro and white infants. In our series of infants with normal M.C.H.C.s the difference between the mean haemoglobin levels of the two races rose from 0.7 g./100 ml. in the 5 to 7 months group, to 1.6 g./100 ml. in the 11 to 13 months group; thereafter it decreased to 0.6 g./100 ml. by 20 to 23 months. Munday *et al.* (1938) found a difference between the mean haemoglobin levels of negro and white infants of 0.5 g./100 ml. at 4 months, rising to 1 g./100 ml. at 13 months. Similarly, the mean haemoglobin levels at the age of 1 year in Munday's series were 11 g./100 ml. for the white and 10.5 g./100 ml. for the negro infants, while our values at this age were 10.9 and 9.1 g. respectively. As the nutrition of Munday's infants was carefully supervised, dietary deficiency was an unlikely aetiological factor in his series.

A surprisingly high incidence of iron deficiency was found in the European infants (22.4%), while the incidence of anaemia was very much higher in the West Indian group (53.5%). No simple explanation for this difference in incidence between the two races could be found. There was no evidence to suggest that prematurity, excessive growth, malnutrition, or the presence or absence of eczema was responsible. The failure to find ova in the stools eliminated intestinal worms as a factor, and the satisfactory response to oral iron made severe malabsorption an unlikely cause. The possibility of inadequate diet or deficient iron stores at birth was considered. Although detailed dietary surveys were not carried out there seemed to be little difference between the diets of the two races or in the time at which mixed feeding was started. Furthermore, all the children attending the day nurseries received the same diet for five days of the week. While dietary factors may have played some part in the older children, they are unlikely to have accounted for the differences found in the infants aged 5 to 7 months. In this age-group an M.C.H.C. below 30% was found in five out of seven West Indian infants but in only one out of twelve European infants. Thus, at the end of the first five to seven months of life many more of the West Indian infants were already iron-deficient, and in the preceding period the diet of both races would have consisted almost entirely of milk. Thus it seemed probable that the iron deficiency in this group resulted from diminished iron stores at birth.

Summary

Among infants aged 5 to 23 months the haemoglobin levels and the mean corpuscular haemoglobin concentration were lower in the West Indians than in the Europeans. Atopic eczema did not contribute to this difference, since similar haemoglobin levels were found in the healthy and eczematous infants.

Iron-deficiency anaemia, indicated by an M.C.H.C. of less than 30%, occurred in 22.4% of the European and in 53.5% of the West Indian infants.

Such a striking difference could not be explained by prematurity, excessive growth, malnutrition, or the presence of worms. Furthermore, the satisfactory response to oral iron excluded any obvious absorption defect.

While deficient iron intake may have played a part in the older infants it would not have accounted for the high incidence of iron deficiency in the West Indians aged 5 to 7 months; in these infants diminished iron stores at birth may have been responsible. Even when the M.C.H.C. was normal, haemoglobin levels were lower in the West Indians than in the Europeans. This suggested an inherent racial difference in haemoglobin levels in this age-group.

We thank Dr. W. H. S. Wallace, the L.C.C. Divisional Medical Officer, for allowing us to study children at the day nurseries, and the matrons and staffs of these nurseries for their willing co-operation. We are indebted to Miss J. I. Silk, Miss M. Mundy, and Miss T. Smith for technical assistance. Finally, we are grateful to Professor W. M. Davidson for his advice.

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INCOMPLETE ANTI-O IN A PREGNANT MOTHER

BY

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Naturally occurring anti-O, complete and bivalent in type, has been demonstrated by many workers (Landsteiner and Witt, 1926; Henry, 1946; Boorman, Dodd, and Gilbey, 1948). Morgan and Watkins (1948) differentiated anti-H from true anti-O by agglutination inhibition technique. Agglutination of group O cells with anti-H was inhibited by saliva of secretors, but that produced with anti-O agglutinin remained unaffected. Bhatia and Bhende (1954) demonstrated that H-agglutinogen was antigenic to rabbits, but completely mutated O antigen failed to produce any antibody. While investigating a woman with a history of stillbirths, an incomplete type of anti-O was detected in her serum towards the later months of pregnancy. The details of the investigations on this patient are presented below. A similar instance of an incomplete type of anti-O was first demonstrated by Mollison (1959) in a group A patient.

Case Report

A woman aged 34 was first examined on October 10, 1958, during the sixth month of pregnancy. She was

delivered by caesarean section on January 21, 1959. The child was underweight but otherwise normal, and was alive and well at the time of writing.

Obstetrical History.—The patient was married in 1944 and had had four pregnancies. *First pregnancy* (1948): toxaemia; full-term forceps delivery; baby stillborn. Cause of death could not be ascertained. *Second pregnancy* (1950): baby stillborn, post-mature (17 days); normal full-term delivery. Cause of death unascertained. *Third pregnancy* (1952): full-term female baby, delivered by caesarean section because of placenta praevia and unfavourable obstetric history. Baby living and in normal health. Mother came under investigation at the fourth pregnancy.

Blood.—The patient had not received any previous blood transfusion. Group A_1 CDE MN, non-secretor. The cells showed agglutination with natural anti-H serum, signifying the presence of H-substance. Serum showed agglutination with all the group O cells in albumin medium but not in saline. The serum was also tested with A_1 and A_2 cells, both of Rh-positive and negative types. The results obtained are shown in the Table.

Results of Serum Tested with O, A_2, A_1 Cells at 37° C.

Medium Used	Group O			Group A_2			Group A_1		
	Total No. Tested	Agglutination		Total No. Tested	Agglutination		Total No. Tested	Agglutination	
		Yes	No		Yes	No		Yes	No
Albumin	40	40	Nil	8	2	6	32	Nil	32
Saline	40	Nil	40	8	Nil	8	32	,,	32

The antibody was best demonstrable at 37° C. At 22° C. the reaction was feeble. The titre of the incomplete antibody in the serum during the later part of the antenatal period varied from 2^3 to 2^4 up to the confinement. Indirect Coombs tests with group O and A_2 cells were negative. The serum was not tested with enzyme-treated cells. Both the W.R. and the V.D.R.L. test of the serum were negative.

Inhibition Tests.—Agglutination inhibition tests were carried out with saliva of secretors—six from group O, four from group A, and two from group AB persons. In every case the action of the albumin-acting antibody on group O cells was not altered by addition of saliva. The results were compared with known anti-H serum.

Examination of Newborn Baby.—Female child, born at full term—weight 4 lb. 2 oz. (1,870 g.). Blood: Group A_1 CDe MM; haemoglobin, 17 g./100 ml.; osmotic fragility—normal, started at 0.44% and completed at 0.34% of sodium chloride solution; reticulocytes, 3.5%; serum bilirubin, 3 mg./100 ml. of plasma. Direct and indirect Coombs tests were negative in different dilutions. The cells showed no agglutination with mother's serum or even in albumin medium. No sign of haemolytic anaemia was obtained at birth.

The husband was group O CDe MM, non-secretor. The cells showed agglutination with mother's serum only in albumin medium.

Child of Third Pregnancy.—Female, living, healthy, aged 9 years. Blood: Group A_1 CDe MM; the cells do not show any agglutination with mother's serum or even in albumin medium.

Discussion

The antibody found in the mother's serum was active only in albumin medium. In Mollison's case antibody was most active at 25° C., whereas in the present case the optimum temperature was found to be 37° C. The antibody agglutinated all the group O cells and two of the group A_2 cells, but none of the A_1 cells tested. As the mother belonged to CDE MN type, she could not develop any antibody against these antigens. The mother's cells showed agglutination with anti-H serum, signifying the presence of H-substance in her erythrocytes. No anti-H could be obtained in her serum, indicating that she belonged to incomplete mutated type. By agglutination-inhibition technique with the saliva from 12 secretors it was demonstrated that the activity of the mother's serum against group O cells remained unaffected. The selective activity of the serum on group O and A_2 cells which was not affected by saliva from secretors proved that the antibody in question was anti-O and not anti-H.

It is difficult to explain how this incomplete anti-O appeared in the serum of this patient. Either the antibody was naturally present in the mother's serum or it had appeared owing to iso-immunization by the heterozygous AO cells of the foetus. Incomplete antibody appears in the serum by the process of iso-immunization, but occasionally it remains naturally in the serum of some individuals. Ervin and Young (1950) reported the presence of incomplete anti-A in two group O donors; one was a group O male, and the other a group O female whose husband belonged to group O. Both these individuals were dangerous universal donors. Zuelzer and Kaplan (1954) reported the presence of immune anti-A in two cases of homospecific pregnancy. The nature of the possible antigenic stimulus in both cases was obscure.

Whatever may be the source of origin of this incomplete anti-O, no sign of haemolytic disease was obtained in the baby of the fourth pregnancy. The causes of neonatal death in the first and second pregnancies were not known to us.

Summary

Incomplete anti-O was present in the serum of a mother towards the later months of pregnancy. The mother belonged to group A_1 CDE MN, and was a non-secretor of A-substance.

Antibody showed agglutination with all group O cells, both Rh-positive and Rh-negative, and two out of eight A_2 cells only in albumin medium.

The mother's cells showed agglutination with anti-H serum of animal origin.

Addition of saliva of secretors six from O, four from A, and two from AB did not alter the effect of antibody on group O cells.

The antibody was more effective at 37° C.

We are grateful to Dr. R. R. Race, Director, Blood Group Research Centre, Lister Institute, London, for kindly confirming our opinion regarding the presence of incomplete anti-O antibody. We thank Dr. J. B. Chatterjea, professor of haematology, School of Tropical Medicine, Calcutta, for kindly confirming our findings.

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A striking increase in the prevalence of epidemic hepatitis in Poland is reported. The number of cases registered has risen from 26,000 in 1957 to 43,000 in 1958 and 75,000 in 1959. W.H.O.'s Regional Office for Europe has been asked to assist studies in the prevention of this disease.

Medical Memoranda

Localized Amyloid "Tumour" of Larynx Preceding Rheumatoid Arthritis

[WITH SPECIAL PLATE]

Amyloid "tumours" of the larynx are rare lesions and were first described by Burow and Neumann (1873) as being found at necropsy. Accounts in English are few, and Thoma in his authoritative textbook makes no reference to the condition. The majority of references are German. Herxheimer (1903) published an extensive collection of cases. Pollak (1914), in a review of idiopathic amyloid deposition in the upper air-passages, listed its characteristics—multiple lesions in the organ involved; involvement of contiguous tissues; waxy appearance of the tumours; absence of pain, lymph-node involvement, and ulceration of overlying mucous membrane. Some of the cases since published had single lesions confined to the larynx, as in the present instance, but others, such as those of Kramer and Som (1935) and McCall and Fisher (1953), had multiple laryngeal lesions but none elsewhere. The association with rheumatoid arthritis of amyloid deposits having a distribution similar to that of secondary amyloidosis has been reported by several authors (see Missen and Taylor, 1956). The present case is most exceptional in that rheumatoid arthritis only developed four years after the appearance of a localized amyloid deposit in the larynx.

CASE REPORT

A woman of 40 first complained of progressive hoarseness and pain radiating up the left side of the neck into the face in 1954. These symptoms were progressive. She was first examined in 1955, and on indirect laryngoscopy a smooth mass, over which the mucosa was intact, was seen expanding the left aryepiglottic fold from the vestibular band to the base of the epiglottis. The vocal cords were normal. No lymph nodes were palpable, and the sputum was negative for tubercle bacilli. Wassermann reaction negative. The congo-red test for amyloidosis gave results within normal limits. She gave a long history of asthma, and was discovered to have dermographia. There was no demonstrable focus of chronic suppuration. Laryngeal tomography in April, 1956, showed the outline and position of the mass (Special Plate, Fig. 1). A biopsy specimen (Dr. A. G. Heppleston) contained much amorphous material situated intercellularly and showing the tinctorial reaction of amyloid. The amyloid tended to occur as small masses separated by fibroblasts and chronic inflammatory cells. There was a prominent giant-cell reaction to the amyloid and some masses were surrounded by these cells, but they did not appear to have ingested amyloid (Special Plate, Fig. 2). Serous glands were included in the amyloid "tumour." The symptoms were unaffected by the biopsy, and she was discharged.

In August, 1958, her symptoms were unchanged and the mass was still present, though little increase in size was discernible tomographically. Owing to the persistent hoarseness the patient pressed for removal of the mass, though there was no stridor. This was done through a thyroid fissure. Histological examination showed a large amount of material resembling amyloid, but the cellular reaction was now much less intense and few giant cells occurred. After two weeks she was discharged.

There has been no definite laryngeal recurrence up to February, 1959, but granulation tissue remains on the anterior end of the false cord near the site of the original lesion. Pain has completely disappeared. In November, 1958, three months after the operation, she developed for the first time typical signs of rheumatoid arthritis, affecting hands, knees, and ankles, and these manifestations are still present.

COMMENT

Most authors classify amyloid disease on a similar basis (Dahlin, 1950; Symmers, 1956): (1) primary amyloidosis—systemic—local; (2) amyloidosis complicating myeloma—systemic—focal; (3) secondary amyloidosis; (4) amyloidosis associated with rheumatoid arthritis.

Localized amyloidosis is to be regarded as a primary type in that there is no associated suppuration and the staining reactions are weak or absent. It is most common in the larynx and trachea. It may also be found in the nose, pharynx, tongue, bladder, urethra, and eye (Reimann *et al.*, 1935). New (1919) has further subdivided the localized amyloid deposits found in the larynx: (1) diffuse subepithelial infiltration; (2) tumour forming local amyloidosis; (3) amyloid degeneration in a pre-existent tumour. This subdivision is useful when the question of treatment arises, as it is obvious that the same treatment will not apply to all types, the diffuse being unsuitable for radical surgery.

Primary localized amyloidosis of the larynx tends to appear slowly, and, though described as a "tumour," amyloid in reality appears as an infiltrate in the affected organ. It is intercellular and has no intrinsic cellular activity of its own. Stark and New (1950) suggested that the disease in the larynx tends to be self-limiting. Tomographs of our case taken at almost three years' interval show that there has been little increase in size of the tumour. Single amyloid tumours of the larynx cause symptoms by mechanical interference, and the severity therefore depends on the size and site of the lesion. In the absence of a lesion on the vocal cords or of narrowng of the airway the disease may remain occult for years.

The lesion must be distinguished from other simple and malignant tumours. Final diagnosis rests on biopsy, which usually has no apparent effect on the amyloid mass. Pollak (1914), however, reported regression of an amyloid tumour of the larynx after simple biopsy, while Kramer and Som (1935) appear to have stimulated enlargement of a similar tumour by diagnostic biopsy. Intravenous injection of congo-red will stain the tumour deep pink, showing clearly its extent, which is of value when surgical removal is attempted.

Stark and New (1950) favour surgical removal of the well-defined tumour whatever its position. The response to deep *x*-ray therapy appears to be unpredictable. Cortisone and corticotrophin represent the most recent mode of treatment, but the response is not consistent.

Missen and Taylor (1956) found eight cases of secondary amyloidosis in 47 cases of rheumatoid arthritis. They do not describe a single lesion in the larynx, and in all cases the amyloid appears to have followed rheumatoid arthritis. The primary lesion in the present case was a single localized amyloid deposit in the larynx, which is in sharp contrast to the usual distribution of amyloid in cases of rheumatoid arthritis; moreover, the symptoms of rheumatoid arthritis did not appear until four years after the onset of laryngeal symptoms, and this appears to be unique. The appearance of amyloid has been imputed to an abnormality of protein metabolism. It is thought that

amyloid might be formed when chondroitin-sulphuric acid released from the breakdown of cartilage or elastic tissue was combined with protein. The frequency with which secondary amyloidosis and hyperglobulinaemia occur together lent weight to the idea. Loeschcke (1927) regarded amyloid as an insoluble precipitate of antigen and antibody. Hüsselmann (1955) suggested that in primary amyloidosis muscle might act as an auto-antigen, with the eventual occurrence of an antigen–antibody reaction in muscle tissue, the outward and visible sign of which is amyloid deposition. No consistent relationship has been reported between primary amyloidosis and allergic manifestations. In a case reported by Lindsay (1946) there was an allergy to egg-white protein, and Findley and Adams (1948) mention an allergy to pollen. The present patient has asthma and dermographia, and, though the association with amyloidosis and rheumatoid arthritis may be fortuitous, it is tempting to suggest that all four manifestations have an immunological or hypersensitivity basis. There is, in fact, presumptive evidence of an immunological mechanism in amyloidosis (Vázquez and Dixon, 1956) and in rheumatoid arthritis (Vázquez and Dixon, 1957).

My thanks are due to Mr. R. D. Owen and Mr. A. B. Thomas for their permission to publish this case and for their help in the preparation of the paper; also to Dr. A. H. Heppleston, of the Pathology Department of the University of Wales, for his advice and the reports on the sections, and to Mr. R. J. Marshall, of the Photographic Department.

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"Once again the usual crop of foreign bodies was encountered. Fragments of glass, a nail, an adhesive bandage, and a flour sack tag were all identified in samples of bread or cake; bakery dirt and mould were also confirmed in other instances of bread and meat pies. Possibly the most revolting was the identification of two large spiders in a bottle of pasteurized milk. Vinegar eels, which are harmless but rather alarming-looking organisms, were detected in a sample of vinegar. Most vinegar nowadays is pasteurized, and this sort of contamination, once common, is not often encountered. Fermentation had produced a 'bubbly' sample of herrings in vinegar which blew off the lid when the container was opened. Crystals found in a can of tuna fish proved to be struvite crystals (composed of magnesium ammonium phosphate derived from the natural constituents of the fish), which are quite harmless." (Birmingham City Analyst's *Report for the Second Quarter, 1960.*)

Reviews

NITROUS OXIDE IN DENTAL ANAESTHESIA

Nitrous Oxide in Dentistry. Its Dangers and Alternatives. By J. G. Bourne, M.A., M.D.(Cantab.), F.F.A. R.C.S. (Pp. 181+x; illustrated. 30s.) London: Lloyd-Luke (Medical Books) Ltd. 1960.

A sure way to make progress in medicine is to take some item of everyday routine, accepted by everyone, and about which there seems little prospect or even need of change. When such an item is re-examined critically in the light of up-to-date knowledge and methods of investigation, exciting prospects soon become visible and drastic changes will appear to be indicated. Dental anaesthesia is an example of such an everyday procedure which is long overdue for re-examination. However, fruitful ideas for improvement in this field are not likely to come from committees but from individuals who, with an original turn of mind and a disinclination to accept "proof by authority," are prepared to give up methods which by other standards should be discarded.

Bourne's book makes an original and angry attack on the commonly used method of chairside dental anaesthesia. Although it is an expanded version of an M.D. thesis, the very vigour of its presentation makes it a descendant of the campaigning pamphlets of over a century ago which in their time were responsible for so much important social and scientific change.

Apart from the speed of induction, the brief duration of its effects, and the speed of recovery from it, nitrous oxide has really little to recommend it for routine use in the dental chair. Because of its low potency, the danger of hypoxia is often inseparable from nitrous oxide anaesthesia, and this was already pointed out by Courville nearly 25 years ago. Bourne summarizes a mass of further evidence on this point which has accumulated since then. Nitrous oxide is perhaps not as "safe" and "non-toxic" as many would have it. In addition, the jactitations of the patient if he is hypoxic, or his reflex movements to pain if he is not, withhold from the dental surgeon the calm atmosphere and immobile patient to which he is as entitled as his colleagues in the surgical field.

Bourne discusses with great clarity the physical, chemical, and physiological factors which determine whether an anaesthetic is potent, of speedy onset, and quickly recovered from. The conclusion leads him to cyclopropane as a more suitable anaesthetic than nitrous oxide. The one disadvantage of flammability is removed by mixing the gas with an inert diluent to render the mixture non-flammable.

The reviewer found this book packed with interesting information and good argument. To read it is an exciting experience, the vigour of Dr. Bourne's style and the persuasiveness of his logic being unusual in books of this sort. If the reader's brow wrinkles occasionally at references to "fainting" under anaesthesia, he should be patient, for near the end he will find an extended explanation of this term in a discussion on vaso-vagal reflexes. Bourne makes a real and constructive contribution towards safer and more effective dental anaesthesia. If his critical and vigorous approach is emulated by others, a new era in this field may well be round the corner. No one who is interested in dental anaesthesia should fail to read this important book.

W. W. MUSHIN.

CHEST TUMOURS

Diagnosis and Treatment of Tumors of the Chest. Sponsored by the American College of Chest Physicians. Editor-in-Chief: David M. Spain, M.D. (Pp. 371+xii; illustrated. $14.75.) New York and London: Grune and Stratton. 1960.

This book, sponsored by the American College of Chest Physicians, gives a comprehensive account of all forms of tumours of the chest, each section being written by a separate author under the general editorship of Dr. D. M. Spain.

As might be expected, cancer of the lung occupies a considerable amount of space, and there are informative chapters on the aetiology and pathogenesis of the disease. No feature is overlooked, and in some parts there is a fairly detailed analysis based on the experience of the individual author. For example, in assessing the five-year survival rate of more than 100 patients who had a growth excised it was found that an 80% survival could be expected if neither blood vessels nor lymphatics were invaded. The chance of success with lymphatic invasion reduced the figure considerably, but not as severely as if the blood vessels had been invaded.

The description of benign tumours of the lung is adequate, and when dealing with mediastinal tumours the chapter by Dr. Lyons contains a great deal of valuable classified information. In a list of nearly 800 cases many inflammatory and granulomatous conditions are included, but of the more genuine tumours it is interesting to find 26 thymic growths recorded but only 15 neurogenic tumours, which is a considerably lower proportion than thoracic surgeons, at any rate, might expect. In the discussion on lymphomas there is a useful appraisal of the efficacy of chemotherapy.

The account of tumours of the chest wall, which is contributed by the Ochsners, should make a useful source of reference for those interested in this particular subject. It has an exhaustive classification, whereas only a limited amount is said about tumours of the oesophagus. There is an admirably illustrated section on tumours of the heart where the angiograms are numerous and well chosen.

Dr. Spain's contribution on the systemic manifestation of disease at the end of the book affords a suitable reminder that the study of diseases in one site cannot be made without reference to the whole organism.

In spite of a multiplicity of authors the book is well balanced and covers a great deal of ground, and the illustrations and production leave little to be desired.

T. HOLMES SELLORS.

FREEZING AND DRYING

Recent Research in Freezing and Drying. Edited by A. S. Parkes, C.B.E., F.R.S., and Audrey U. Smith, D.Sc., M.B., B.S. (Pp. 320+vii; illustrated. 63s.) Oxford: Blackwell Scientific Publications. 1960.

No field of science has developed more rapidly than that concerned with the long-term preservation of the integrity of biological material, ranging from subcellular derivatives and particulates to complete organisms or their component tissues and organs. At least five international conferences have been devoted to freezing and drying since 1951.

Within less than eight years we have seen methods developed, more or less empirically, which either now are, or could easily be, employed on a large scale for the long-term storage of a wide variety of mammalian cells and tissues and micro-organisms at very low temperatures in what is effectively a state of suspended animation. Low-temperature preservation of bull spermatozoa and of tumour cell lines are common practices in animal husbandry and cancer research respectively. These were made possible largely by application of the accidental discovery that glycerol exerts a protective action against the otherwise harmful effects of freezing, and by empirical determination of optimal rates of freezing and thawing. A few years ago contributions of biophysicists were not infrequently frustrating or misleading, since they either required conditions of cooling that could not be realized in practice or made predictions in complete disagreement with existing experimental observations. The 21 papers included in the present volume, presented at the symposium organized by the Institute of Biology in 1958, give a valuable and well-balanced picture of the present status of the field and leave no doubt that a happy marriage between fact and theory has now taken place.

Studies on the process of ice-crystal formation in aqueous solutions and in animal cells and tissues are described that sustain the thesis that a major cause of cell injury during freezing is the indirect outcome of ice-crystal formation—the concentration of electrolytes. The protective action of glycerol is explained, and various contributors report progress in finding substitutes for it, or in devising regimens of cooling obviating the need for protective agents. Protective agents, so valuable during the course of deep cooling, may become an embarrassment when this is to be followed by desiccation, especially with non-volatile substances like glycerol.

Purely theoretical aspects of the mechanics and physics of freezing and drying are well covered, including the design of equipment. Nine of the papers are principally concerned with the effects of cooling and desiccation on micro-organisms, including yeasts and B.C.G., with a view to storage with minimal loss of viability. Four papers deal with the employment of various stored tissue homografts in surgery and evaluate methods of procurement and preservation in relation to therapeutic results. The concluding paper, by Dr. Parkes, deals with the intriguing possibility of being able to freeze-dry mammalian tissue grafts with retention of viability—concerning which both he and other contributors display cautious optimism. The book is attractively set out with clear illustrations and provided with an excellent index.

R. E. BILLINGHAM.

CHRONIC ILLNESS SURVEY

Chronic Illness in the United States. Volume III. Chronic Illness in a Rural Area. The Hunterdon Study. Reported by Ray E. Trussell, M.D., M.P.H., and Jack Elinson, Ph.D. (Pp. 440+xiv. 60s.) Cambridge, Mass.: Harvard University Press (Commonwealth Fund). London: Oxford University Press. 1959.

This is the third of the four volumes published by the American Commission on Chronic Illness which was established in 1949 and now completes its task. Understandably it is the last to be printed, for the difficulties in getting the work done must have been immense. The area surveyed, Hunterdon County in the State of New Jersey, covers 435 square miles; its population is a little more than 40,000, but it has no

fewer than 26 independent municipalities each responsible for its own educational and health needs. Not surprisingly there is no organized health service, but a county "Medical Center" was established a few years ago; there are no hospitals, no laboratories, no health department, and no medical specialists. The technique of the survey was developed in four phases. The first step was the circulation of 43,000 twelve-page questionaries, and 56% of these were completed and returned. Next, family interviews were arranged. Each adult was seen separately, and to "the one best informed" particular attention was given. Letters were then sent to family doctors for confirmation or elaboration of statements made at the interviews, and no less than 86% of them replied. Finally, complete clinical investigations were conducted by teams approved by New York University and supported by the usual "battery of tests."

It was shown that the incidence of chronic disease in this rural area was much higher than had been expected; nearly everyone over 45 had something wrong. Six per cent. of the disease processes might have been prevented entirely, but many more could have been arrested and relieved by suitable treatment. Comparison of the principal defects with those found by the survey in the city of Baltimore shows an almost identical pattern in both, but obesity in the rural area was more conspicuous. The incidence of mental disorder in Hunterdon was actually slightly greater than in Baltimore, and this does not suggest that "the strain of city life" has much to do with the onset of psychoneurosis.

The clinical teams found no difficulty in reaching agreement on the extent and nature of the conditions revealed by the survey, but they remained hopelessly divided about the remedy. Who should supply the care and assistance that were obviously needed? And how much and what sort of care should be afforded? These questions and their answers are matters of social policy; medicine can do no more than define the problem.

A. P. THOMSON.

ANTIBIOTICS

Antibiotic Therapy for Staphylococcal Diseases. Edited by Henry Welch, Ph.D., and Maxwell Finland, M.D. Foreword by Felix Martí-Ibáñez, M.D. (Pp. 208+xii. $4.50.) New York: Medical Encyclopedia, Inc. 1959.

A Guide to Antibiotic Therapy. By Henry Welch, Ph.D. (Pp. 69.) New York: Medical Encyclopedia, Inc. 1959.

The volume edited by Welch and Finland is arranged in an unusual way. The first chapter, by Welch, is on the general problem of staphylococcal infections and their treatment with penicillin, chloramphenicol, tetracyclines, or bacitracin. Then follow six chapters on other individual antibiotics by different authors, among which that on oleandomycin is twice as long as any of the others, these being on erythromycin, novobiocin, vancomycin, ristocetin, and kanamycin. These chapters are fully documented and should be valuable sources of detailed information on the newer and less generally familiar drugs. Finally, Finland restates the problem on a basis of wide and direct experience, compares the properties of all the foregoing antibiotics which determine or limit their usefulness, and defines the principles which should direct the treatment of staphylococcal infections. This authoritative summing-up is the best part of a rather uneven book.

Welch's *Guide* is even more unusual, since it has no text in the ordinary sense. A pair of facing pages is given to each of 31 antibiotics, the inner columns being devoted to "general indications," "side effects," and "dosage forms," and the outer to tables of minimum inhibitory concentrations for 37 species or genera of bacteria, 11 of fungi, and a few viruses, rickettsias, and protozoa. No references are given; it would be helpful if the authority for some of the data were cited. Three figures, headed "low," "high," and "majority," are listed in each entry; these—in μg./ml.—are given, for instance, for tetracycline against *Staph. aureus* as 0.05, 250, and 7.5. This "majority" figure—and many of the others quoted, e.g. 5.0 for tetracycline against clostridia and *H. influenzae*, and for streptomycin against *Myco. tuberculosis*—is discouraging and unhelpful. Would it not be better to state the minimum concentration to which the organism is normally sensitive, which is ten to fifty times lower than the "majority" figure given in all the examples cited, and let the reader supply information about the frequency of resistance from his local knowledge?

We must nevertheless be grateful for the presentation of so much information in a condensed form; anyone really ignorant about the properties of an antibiotic (and almost anyone may be about such antibiotics as "hygromycin" and "thiostrepton") can get some idea of its sphere of possible usefulness from these tables.

L. P. GARROD.

AMERICAN PSYCHIATRY

American Handbook of Psychiatry. In two volumes. Editor: Silvano Arieti. Editorial Board: Kenneth E. Appel, Daniel Blain, Norman Cameron, Kurt Goldstein, and Lawrence C. Kolb. (Pp.: Vol. I: 999+xix; Vol. II: 1,000–2,098+ix; illustrated. £10 10s.) New York: Basic Books, Inc. London: Mayflower Publishing Co., Ltd. 1959.

The progress of psychiatry has perhaps been retarded in Britain by the lack of comprehensive textbooks such as those monuments to Teutonic thoroughness, the handbooks of Bumke or Kraepelin. It was hoped, therefore, that this major work would fulfil a much-felt need. There are 100 chapters by 111 authors, many of whom are authorities in their respective fields. A glance through the contents reveals a glittering constellation of ability; Kallman on genetics, Goldstein on brain damage, Ruesch and Spiegel on communication theory, Moreno on psychodrama, Freeman on psychosurgery, and Papez on neuro-anatomy, to mention only a few. The *Handbook* is also remarkable for its comprehensiveness. As well as the subject matter ordinarily covered in a psychiatric textbook, there are chapters on existentialism, cybernetics, psychiatry and philosophy, religion (Protestant, Catholic, Jewish, and non-Western), psychiatric nursing, family care, and the teaching of psychiatry. There are also chapters on neuro-anatomy, neurophysiology, neurology, and neuropathology, which are perhaps the weakest part of the book and which would have been better either omitted or expanded. The authors of these chapters were given an impossible task to deal with their vast and complex subjects in a few pages.

The defects of the book for the British reader are that it does not reflect psychiatry as practised in this country. There is too great an emphasis on psychodynamics in the aetiology and treatment of the psychoses, and it comes as a welcome relief, like a breath of fresh air into the miasma of platitudes ("physical therapies produce

only a symptomatic relief whereas psychotherapy tends to (1) remove the basic conflicts which led to the disorder (schizophrenia), (2) correct the psychopathologic patterns, et cetera"), when Bruetsch trenchantly states, of G.P.I., "If treatment with antibiotics should result in a failure, psychotherapy will not benefit the patient either." There is, also, too much emphasis for the British taste on early upbringing. Moreover, much of the book is applicable only to the U.S.A.—methods of committing a patient in various States, the organization and teaching of psychiatry, and so on. But this is hardly a fair criticism: after all, the book is an *American* handbook of psychiatry. This probably accounts for the fact that most of the references are from American literature.

The defects of the book are those of American psychiatry where the dichotomy between the psychotherapists (orientated to private practice) and the somatotherapists (orientated to State hospital economy) is so much more marked than in this country. These different approaches are indeed presented, and "a guiding principle in the organization of the handbook was that of preventing a check and balance between different approaches." Different approaches, by so many authors, make it difficult for the editor to make the book what he would call holistic and organismic.

The good point of the book is that much valuable material is here collected in a convenient if weighty form, much of which is not otherwise readily available. It is not to be recommended to the novice in psychiatry, but experienced practitioners can derive much profit from these volumes.

A. W. BEARD.

EVERYDAY PROBLEMS

Reflections of a Medical Investigator. Four Lectures Delivered at the University of Groningen. By R. A. McCance, C.B.E., F.R.S. (Pp. 63; illustrated. 7s. 6d.) London: Pitman Medical Publishing Co. Ltd. 1959.

This little book is a reprint of four lectures delivered at the University of Groningen in the summer of 1958. They are a good example of the author's ability to do original work on everyday problems, and to write about his results, and those of others, in an attractive way. In the first lecture he deals with "the patient and the doctor," and after commenting on the changing scene in medicine goes on to discuss the experimental approach to medicine and the relation between the patient and the investigator. The second lecture deals with "the food we eat" and leaves one in little doubt that there must be a connexion between the rise in consumption of saturated fats and the fall in consumption of unsaturated fats on the one hand and the increase of coronary thrombosis on the other. In the third lecture, on "calories," McCance stresses the wide variation in intake of food and expenditure of energy in people doing the same kind of work and deplores the recent neglect of the study of calories. Incidentally he mentions that he himself bicycles 80 km. a day, which was doubtless an inspiration to his patient whose weight was reduced from 265 to 75 kg. and who now bicycles 100 km. a day. The last lecture is on "stability and steady states in the newborn animal." Research in this field is so active as to be difficult to summarize briefly, but its main theme is the remarkable ability of the newborn to survive. The book is a paperback and makes agreeable reading for a journey.

L. J. WITTS.

LOCOMOTOR DISORDERS

Diagnosis in Locomotor Disorders. By Kenneth Stone, D.M.(Oxon.), M.R.C.P. (Pp. 224; illustrated. 25s.) London, New York, Toronto: Oxford University Press. 1960.

In his preface the author states that his aim in writing this book is to provide practitioners with a concise work, restricted to essentials, for quick and easy reference. The differential diagnosis in disorders of the locomotor system presents difficult problems, which, he says, as they appear in so many different fields of medicine, are not readily found in any other similar textbook. The book consists of short descriptions of symptoms and signs arranged alphabetically, with a discussion of the differential diagnosis in each case: choreiform movements, for instance, "occur in rheumatic chorea (Sydenham's chorea), Huntington's chorea, and hysteria." A page is then devoted to the first and three lines each to the other two. Backache is not listed in the index, nor is lumbago, but pain in the back is. It is a brave attempt to condense a vast amount of bedside knowledge into a small handbook of ready reference. Such a large subject cannot really be so condensed; irregularities are bound to occur and the quick-reference falls down repeatedly. The busy practitioner looking for "neck stiffness" or "neck rigidity" will not find it, though he will find "fibrositis," "cervical cord tumour," and a number of other disorders of this part of the anatomy.

In such a short, compressed book the author has to be dogmatic, and many of his statements will not be accepted by other workers in the same field as giving the whole truth and nothing but the truth. Hypertrophic osteo-arthropathy, for instance, is defined as a syndrome of clubbing of fingers and toes, chronic periostitis at the distal ends of the long bones, and arthritis. "Notably it complicates suppurative conditions, such as bronchiectasis, lung abscess and empyema." Polyarteritis nodosa, Hodgkin's disease, idiopathic steatorrhoea, and a number of other conditions are also said to cause this syndrome. The frequency with which it occurs with bronchial carcinoma is, however, also stressed, but throughout this section simple clubbing and hypertrophic osteo-arthropathy tend to be confused.

In spite of all these criticisms, the author has written a book which does cover a lot of ground and contains much information in concise form for the practitioner with little time for more detailed reading.

F. DUDLEY HART.

MENTAL SUBNORMALITY

Mental Subnormality: Subnormality and Severe Subnormality. By W. Alan Heaton-Ward, M.B., Ch.B., D.P.M. (Pp. 64; illustrated. 6s.) Bristol: John Wright and Sons, Ltd. 1960.

There is still a dearth of reliable literature on mental retardation, and Dr. Heaton-Ward's booklet will be welcomed by the school medical officer and others working in the field as providing a short guide to the new Mental Health Act as well as a brief outline of some of the main problems in the care of the backward. The treatment is necessarily didactic, but reflects some of the advances of recent years. The author does not believe, however, "that there will be any dramatic reduction in the hospital population in the foreseeable future." He points out that the main reduction in numbers of mental defectives under care has been in

those under guardianship. He emphasizes the value of temporary admission to hospital for fuller investigation. Dr. Heaton-Ward points out that "the behaviour difficulties of the subnormal patients are potentiated by their collection together in large groups, and it is desirable that they should be treated in wards for not more than 20–25 patients." Force is added to this view by Tizard's[1] and Lyle's[2] demonstration of the benefit of a small unit.

It would be unfortunate if the very brief treatment in this booklet were to help to perpetuate any of the mistaken beliefs and medical "folklore" with which mental defect has become surrounded. "Simple undifferentiated amentia" is put into the "primary" category. This may lead the reader to believe that if we do not know the cause of backwardness then it must be hereditary in nature. This is far from being the case. Again, we are told that amentia in the subnormal category tends to be perpetuated in the offspring. In a series of 108 children of certified defectives Brandon[3] found a mean intelligence quotient of 91, and only 3.7% of the children were defective. In making genetic prognoses account is not always taken of the fact that in the past a number of those certified as "feebleminded" have been within the normal range of intelligence, nor that the hereditary factors involved in "simple amentia" are extremely miscellaneous. Thus, even if the partner should also be dull, his genetic potentialities may be quite different from those of his spouse. Nor must the big effect of cultural and general environmental factors be ignored.

B. H. KIRMAN.

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BOOKS RECEIVED

Review is not precluded by notice here of books recently received.

The Human Blood Proteins. Methods of Examination and their Clinical and Practical Significance. By Ferdinand Wuhrmann, M.D., and Charlie Wunderly, Ph.D. (Pp. 491+xi; illustrated. $15.75.) New York, London: Grune and Stratton. 1960.

The Fire Escape. By Susan Kale. (Pp. 255. 18s.) London: Putnam. 1960.

Ciba Foundation Colloquia on Endocrinology. Vol. 13. ***Human Pituitary Hormones.*** Edited by G. E. W. Wolstenholme, O.B.E., M.A., M.B., M.R.C.P., and Cecilia M. O'Connor, B.Sc. (Pp. 336+xii; illustrated. 50s.) London: J. and A. Churchill Ltd. 1960.

Disease and the Advancement of Basic Science. Edited by Henry K. Beecher. (Pp. 416+xi; illustrated. £5.) Cambridge, Mass.: Harvard University Press. London: Oxford University Press. 1960.

The Healthy Child. His Physical, Psychological and Social Development. Edited by Harold C. Stuart and Dane G. Prugh. (Pp. 507+xvi. 80s.) Cambridge, Mass: Harvard University Press. London: Oxford University Press. 1960.

Women and Fatigue. A Woman Doctor's Answer. By Dr. Marion Hilliard. (Pp. 174+x. 10s. 6d.) London: Macmillan and Co. Ltd. 1960.

No Crying in this Cradle. The Expectant and Nursing Mother's Bedside Book. By Elizabeth G. Morrison, S.R.N., S.C.M., M.T.S., and Joan Goldman. (Pp. 159+xi. 15s.) London: Ernest Benn Limited. 1960.

Helminthologia. Vols. 1–4. (Pp. 325; illustrated.) Bratislava: Academia Scientiarum Slovaga. 1959.

General Anaesthesia for Dentistry. By Victor Campkin, M.B., B.S., F.F.A. R.C.S.(Eng.), D.A. (Pp. 88+viii: 10s. 6d.) London: Edward Arnold (Publishers) Ltd. 1960.

Preventive Medicine and Public Health. An Introduction for Students and Practitioners. By Fred Grundy, M.D., M.R.C.P., D.P.H. (Pp. 316+viii; illustrated. 27s. 6d.) London: H. K. Lewis and Co. Ltd. 1960.

P-Q-R-S-T. A Guide to Electrocardiogram Interpretation. By Joseph E. F. Riseman, M.D. Fourth edition. (Pp. 168; illustrated. 45s. 6d.) New York and London: The Macmillan Company. 1960.

An Atlas of Human Brain and Spinal Cord Sections. By Hewitt, M.B., B.S. (Illustrated. 5s.) London: Pitman Medical Publishing Co., Ltd. 1960.

The Electrical Activity of the Nervous System. A Textbook for Students. By Mary A. B. Brazier, B.Sc., Ph.D.(London). (Pp. 273+xiv; illustrated. 35s.) London: Pitman Medical Publishing Co., Ltd. 1960.

St. Peter's Hospital for Stone. 1860–1960. Edited by Clifford Morson, O.B.E., F.R.C.S. (Pp. 64+viii; illustrated. 21s.) Edinburgh and London: E. and S. Livingstone Ltd. 1960.

Endemic Goitre. World Health Organization Monograph Series. No. 44. (Pp. 471; illustrated. 40s.) Geneva: World Health Organization. 1960.

Insulin. British Medical Bulletin. Vol. 16, No. 3, September, 1960. London: The Medical Department, The British Council. 1960.

Clinical Disorders of the Pulmonary Circulation. Edited by Raymond Daley, John F. Goodwin, Robert E. Steiner. (Pp. 364+xii; illustrated. 75s.) London: J. and A. Churchill Ltd. 1960.

The Treatment of Tropical Diseases. By W. H. Jopling, M.R.C.P. (Pp. 202+vii. 20s.) Bristol: John Wright and Sons Ltd. 1960.

Patient-centered Approaches to Nursing. By Irene L. Beland and Ruth V. Matheney. (Pp. 205+xi. 31s. 6d.) New York: The Macmillan Company. 1960.

Children for the Childless. Edited by Morris Fishbein, M.D. (Pp. 210+xiii. 12s. 6d.) London: Heinemann. 1960.

Transactions of the Association of Life Insurance Medical Directors of America. Sixty-eighth Annual Meeting. Edited by Whitman M. Reynolds, M.D. (Pp. 266+ix.) New York: Recording and Statistical Corporation. 1960.

Obstetrical and Gynaecological Pathology for Postgraduate Students. By R. E. Rewell, M.D., M.R.C.P. (Pp. 435+xii; illustrated. 50s.) Edinburgh and London: E. and S. Livingstone Ltd. 1960.

Endogenous Endocrinotherapy (Samuels Therapy) including the Causal Treatment of Cancer Compendium. By Jules Samuels. Revised 11th edition. (Pp. 554; illustrated.) Amsterdam: N.V. Cycloscoop. 1960.

French's Index of Differential Diagnosis. Edited by Arthur H. Douthwaite, M.D., F.R.C.P. (Pp. 1,111+xii; illustrated. £6 6s.) Bristol: John Wright and Sons Ltd. 1960.

Mental Health at Home and Abroad. Proceedings of a Conference held at Church House, Westminster, London, March 24-25, 1960. (Pp. 116. 5s. 6d.) London: National Association for Mental Health. 1960.

Education and Retirement. By Brian Groombridge. (Pp. 159. 8s. 6d.) England and Wales: National Institute of Adult Education. 1960.

A Handbook of Diseases of the Skin. By Herbert O. Mackey, F.R.C.S.I. (Pp. 263; illustrated. 8s. 6d.) Dublin: C. J. Fallon Ltd. London: Macmillan and Co., Ltd. 1959.

The Urological Aspects of Bilharziasis in Rhodesia. By R. M. Honey, M.B., F.R.C.S., and M. Gelfand, C.B.E., M.D., F.R.C.P. (Pp. 71; illustrated. 7s. 6d.) Edinburgh and London: E. and S. Livingstone. 1960.

Contributions to Obstetrics and Gynaecology. By V. N. Skirodkar, M.D.(Bombay), F.R.C.S.(Eng.). (Pp. 159+vii; illustrated. 37s. 6d.) Edinburgh and London: E. and S. Livingstone Ltd. 1960.

Cytologie der Cerebrospinalflussigkeit. By Dr. Johannes Sayk, with the collaboration of Professor Dr. Georges Schaltenbrand. (Pp. 175; illustrated. DM. 44.40.) Jena: Gustav Fischer Verlag. 1960.

Better and Better Every Day. By Emile Coué and C. Harry Brooks. (Pp. 158. 6s.) London: Unwin Books. 1960.

BRITISH MEDICAL JOURNAL
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DIGITALIS INTOXICATION

The beneficial effects of digitalis are primarily due to an increase in ventricular efficiency and a decrease in the rate of ventricular contraction. There are, of course, other lesser advantages. Digitalis folia is less often prescribed now than formerly because of its comparatively slow action and very prolonged excretion time. Digoxin is often preferred, but it is equally liable to cause nausea and diarrhoea. Of all the commonly used digitalis preparations digitoxin is the least upsetting to the gastro-intestinal tract.

Ventricular extrasystoles are the commonest of the arrhythmias that may be provoked by digitalis, and, if unchecked, may go on to ventricular tachycardia or even lethal ventricular fibrillation. Digitalis[1] reduces the amount of potassium in cells and this alters the excitability of the ventricles. Moreover, cellular potassium is also known to be reduced in heart failure. Consequently, if the cellular potassium is further depressed owing to diarrhoea and vomiting or to administration of drugs that cause loss of potassium—such as those of the chlorothiazide group or the steroids—there is a risk that the patient's condition will deteriorate and even end fatally.

In the *Journal* this week two teams of investigators describe a further complication of potassium depletion associated with digitalis therapy—namely, atrial tachycardia with atrioventricular block. It is a complication that was described by Lewis in 1909,[1] Mackenzie in 1911,[2] and recently in a book by B. Lown and M. D. Levine.[3] Now Dr. Samuel Oram and his colleagues at King's College Hospital report (page 1402) 11 cases collected over two years in which digitalis is believed to have played the main part in causing atrial tachycardia with atrioventricular block, and Dr. M. F. Oliver and his colleagues at Edinburgh report 18 cases (page 1409).

The dangers of this complication are so great that wide recognition of it is important. If in a patient who has not got thyrotoxicosis an initially high ventricular rate does not fall or actually increases during digitalis therapy, the presence of this arrhythmia must be suspected. Dr. Oram and colleagues draw attention to the need to suspect the presence of atrial tachycardia with A.V. block if the congestive heart failure in a patient receiving digitalis suddenly worsens, or reappears, without obvious cause. And they state that "if careful inspection of the neck veins reveals a jugular a-wave faster than the apical rate the condition is suggested." To distinguish atrial flutter from atrial tachycardia with A.V. block Dr. Oliver and colleagues emphasize a number of points which may be helpful: in cases of atrial flutter the rate of contraction in the atrium usually exceeds 250 per minute and the P waves in the lead II of the electrocardiogram are "saw-tooth" rather than upright and small; in cases of atrial tachycardia with A.V. block the atrial rate is usually 150–200 per minute, and the P waves are upright and small in lead II. However, the distinction may not be clear-cut, and one rhythm may change into the other. In either case pressure on the carotid sinus will increase atrioventricular block, while the atrial tachycardia will be unaffected or revert to normal rhythm.

Atrial tachycardia with atrioventricular block occurs in a few patients who are not receiving digitalis, one case being reported in each of the present papers. The patient of Oliver and colleagues had suffered a recent cardiac infarction, while that of Oram and colleagues had iron-deficiency anaemia and was in hospital after attempting suicide with barbiturates. The dose of digitalis does not appear to be important in the aetiology of the disorder, and Oram and colleagues point out that other signs of digitalis toxicity are uncommon apart from alteration in the ST segment on the electrocardiogram and a few ventricular extrasystoles. Opinion differs on whether most patients who develop atrial tachycardia with atrioventricular block have serious heart disease, but, when they have, it may be possible to administer digitalis to them by giving large doses of potassium after the rhythm has reverted to its previous state.

Treatment of the attack is by stopping digitalis and giving 2 to 8 g. of potassium chloride by mouth each day. Intravenous potassium is usually unnecessary, the majority of patients reverting to normal rhythm without it. For patients not treated with potassium the prognosis is very bad. A wise precaution is always to give potassium supplements to patients who are receiving digitalis and diuretics, especially of the chlorothiazide group, though Oliver and colleagues note that the arrhythmia can arise despite this precaution. "It is all the more important, therefore, that physicians should be alert to this complication of digitalis therapy."

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SURGICAL RELIEF OF PARKINSONISM

Destruction of cells in the ventral lateral nucleus or the caudal ventral nucleus of the thalamus, or destruction of the globus pallidus, or both, can relieve the symptoms of idiopathic or post-encephalitic parkinsonism. These procedures have a contralateral effect. They may be carried out on both sides for patients with bilateral symptoms, though an interval of about six months should elapse before treatment of the second side is undertaken.

The story of this method of treatment begins with the work of H. R. Meyers,[1 2] who tried, among other procedures, the effect of interrupting the efferent fibres of the globus pallidus through the lateral wall of the third ventricle. In some of his patients contralateral tremor and rigidity were abolished apparently without the production of undesirable neurological effects. This operation was based on the observation that the cells of the globus pallidus degenerate in parkinsonism, originally reported by J. R. Hunt,[3] though later observers[4 5 6] found more degeneration in the substantia nigra. More recently, J. G. Greenfield and F. D. Bosanquet[7] observed degeneration to be confined to the substantia nigra in idiopathic parkinsonism, though they found slight degeneration in the globus pallidus in post-encephalitic parkinsonism.

I. S. Cooper,[8] while attempting section of the lateral two-thirds of one cerebral peduncle for contralateral tremor, as described by A. E. Walker,[9] has reported[10] that he inadvertently damaged the anterior choroidal artery and was obliged to coagulate it. (The anterior choroidal artery arises from the internal carotid just above the posterior communicating artery and is adjacent to the cerebral peduncle.) The pedunculotomy was then abandoned, but the patient was found to be free from tremor on the opposite side, and no abnormal neurological signs were produced on this occasion. As a result of this experience, Cooper continued for a time to coagulate the anterior choroidal artery for Parkinson's disease. The beneficial effects were attributed to infarction of the globus pallidus.[11] This operation was soon given up in favour of less risky methods of destroying the globus pallidus, such as injection of procaine in oil[12] and injection of alcohol.[13] In the opening pages of the *Journal* this week Mr. F. J. Gillingham and his colleagues at Edinburgh report on their experience in the treatment of 60 patients by electrocoagulation of the targets. The great majority were much improved. Their mortality was low, two deaths being attributed, at least in part, to the operation.

In this work empiricism has outstripped scientific knowledge and theory. Thus destruction of cells in the ventral lateral nucleus or the caudal ventral nucleus of the thalamus has been found to be more effective than lesions placed in the globus pallidus,[14] though the globus pallidus is still considered by some workers a worth-while target when the effect of lesions placed in the thalamus is not sufficient. There are several ways of locating the nuclei and several ways of inflicting the lesions, but though there is some variation in the position of the nuclei in relation to adjacent cerebral landmarks there can be no justification for magnifying the possible errors by the use of inaccurate apparatus. The use of non-stereotaxic apparatus limits the application of the operation to early and preferably unilateral cases. Thus Cooper[15] finds only one patient in five suitable for his type of procedure. Methods in which there is accurate localization in three planes[16–19] are applicable to most patients with parkinsonism. Especially safe is the combination of the Bennett[19] stereotaxic apparatus and the Oliver[20] cup and ball; the former ensures accuracy to one millimetre and the latter allows gradual destruction of the target zones over several days, for it may be left *in situ* beneath the sutured scalp for the required period.

Restoration of function is the desire of most patients, relief of tremor being of secondary importance,[21] and accurate stereotaxic technique, with graduated destruction of the targets, can restore or improve function in most cases, while tremor and rigidity may be reduced or abolished. Sometimes oculogyric crises and hyperhidrosis are relieved, but dysarthria and ptyalism are not. This technique is applicable to patients of any age with unilateral or bilateral disease provided there is no associated mental deterioration and they are fit enough to stand a light general anaesthetic for a little over an hour in the sitting position.

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21 —— *Parkinson's Disease and its Surgical Treatment*, 1953, London.

MORE RHEUMATISM IN CHILDHOOD

Medicine is ever changing, and the fact that yesterday's disease has gone to-day is no matter for complacency, for it may reappear to-morrow. There has been evidence that the incidence of rheumatism in childhood has declined in recent years to an extent perhaps comparable with tuberculosis, and rheumatic-heart homes and sanatoria have been closed as a result. Now there is evidence that rheumatism is returning, and the letter from Drs. Victoria Smallpeice and Hugh Ellis[1] quoting the Oxford hospital figures will have come as no surprise to paediatricians—either in this country or abroad—for the resurgence of rheumatism appears to be widespread. It is a condition constantly to be remembered when differential diagnosis is concerned.

The symptomatology of rheumatism in childhood is protean; it may appear in the guise of pneumonia, or appendicitis, or a neoplasm such as neuroblastoma, or leukaemia, or as "growing pains." Indeed, the joints may be involved minimally or not at all, just as tuberculosis in childhood may be entirely extrapulmonary. These "variations on a rheumatic theme" underline the lack of exact knowledge of the aetiology of the disease or diseases, though the influence of β-haemolytic streptococci is beyond question. The genetic background has been investigated by M. G. Wilson[2] and her colleagues; it is clear that there is a genetic predisposition in many cases, and that these react with an abnormal response to streptococcal infection and to stress. Diet has for long been known to be a factor in rheumatism, and A. F. Coburn[3] has advised increasing the protein intake, particularly at the expense of carbohydrate, because this was found to decrease the incidence of recurrences in rheumatic children. It may seem a far cry from egg yolk to mitral incompetence, but Coburn's[4] recent work with ethanolamine palmitamide will be followed with the greatest interest.

The diagnosis of rheumatism in childhood is by no means always easy. Acute rheumatism, comparable with the rheumatic fever of adults, presents no great diagnostic problem, but it is perhaps one of the less frequent manifestations in early life. The disease is quite likely to be insidious, at no time showing any obvious signs, yet leading just as surely to carditis as does acute rheumatic fever. Though there is always a preceding streptococcal infection, this may be virtually symptomless, and a history of sore throat may indeed be denied on direct questioning. Further, throat swabs may be misleading, because the offending organism is likely to have disappeared by the time symptoms have arisen, and the absence of haemolytic streptococci in the culture may be wrongly taken as an indication that the illness is not rheumatic. When there is any question of the possibility of rheumatism, the erythrocyte sedimentation rate (E.S.R.) is of the greatest value. In deciding whether symptoms are due to rheumatism it may be taken for granted that the E.S.R. will be raised if they are. For example, if a child with rheumatism complains of pain, and the pain has occurred within three weeks before testing the E.S.R., the rate will be raised; if the E.S.R. is normal, the diagnosis of active rheumatism can be discarded.

Another important test is the estimation of the antistreptolysin titre. In normal children the titre rises for a short time in response to streptococcal infections; in rheumatic children the titre is higher and remains high for longer. Children under the age of 6 years seldom show any great rise,[5] and this is in keeping with the fact that rheumatism is rare in the first six years of life. The E.S.R. and the A.S.T. are both non-specific tests, and raised levels are not necessarily indicative of rheumatic infection, but an antistreptolysin titre of less than 50 units excludes rheumatism.

Clinically the most important and characteristic changes are to be sought in the heart. Tachycardia and a soft apical systolic bruit may be the first signs noted, and the murmur may soon take on a blowing character. Extracardiac signs to be watched for are rheumatic nodules, usually first seen on the extensor surface of the elbow when the arm is fully flexed, and a fleeting, rapidly changing erythema on the back or the front of the trunk—erythema marginatum. Either of these signs is pathognomonic of rheumatism, and nodules usually indicate a severe attack, often with pancarditis. Erythema nodosum may also occur, but, like the E.S.R. and A.S.T., is non-specific. When it is rheumatic in origin it is not usually followed by carditis.[6] Chorea is another frequent extracardiac manifestation of rheumatism, commoner

[1] Smallpeice, V., and Ellis, H., *Brit. med. J.*, 1960, **1**, 1952.
[2] Wilson, M. G., *Pediatrics*, 1948, **2**, 239.
[3] Coburn, A. F., and Moore, L. V., *Amer. J. Dis. Child.*, 1943, **65**, 744.
[4] —— *Lancet*, 1960, **1**, 867.
[5] Rantz, L. A., Maroney, M., and di Caprio, J. M., *Arch. Intern. Med.*, 1951, **87**, 360.
[6] McCarty, M., in *Bacterial and Mycotic Infections of Man*, 1958, Edited by R. J. Dubos, p. 269.

in girls and all too often followed by mitral stenosis.

The importance of a correct diagnosis is directly related to the risk of carditis. It must always be kept in mind that the subacute non-articular forms of rheumatism in childhood are just as apt to lead to carditis as is the classical acute rheumatic polyarthritis; the only difference between them is that the acute form is likely to be recognized more quickly and treatment started forthwith. Bed rest will be accepted without question—but it is no less vital in the subacute form—and, in both cases, should be maintained until the E.S.R. has returned to normal. The value of continuous penicillin prophylaxis is now well established and should be conscientiously followed in all cases, including those children whose hearts are normal. It is, in fact, the rheumatic child with a normal heart for whom the greatest care is necessary, for he may, as a result of this care, enter adult life with his heart still unaffected. The practice recommended at present is to maintain penicillin prophylaxis for at least five years or until after puberty.

MORE ABOUT COMMON COLD VIRUSES

The medical literature contains at least six reports in which the authors claim to have cultivated common cold viruses either in fertile eggs or in tissue culture. In five instances the claims have failed to be confirmed in other laboratories, and any fresh report naturally requires critical appraisal. It is important, therefore, that the most recent claim, by D. A. J. Tyrrell and his colleagues[1] at the common cold research unit at Salisbury, has now received very full confirmation in Sheffield. In this issue (p. 1414) Dr. D. Hobson and Mr. G. C. Schild record that they have isolated viruses similar to the "Salisbury strains" from washings or swabs from 8 out of 25 patients with common colds and not from control material.

The original strains from Salisbury fell into two categories—those growing either in monkey-kidney or human-embryo-kidney tissue-culture (M.K. strains) and those, the large majority, growing only in the latter medium (H.E.K. strains). The special requirements in both groups were that culture tubes were kept rotating in roller-drums, and that they were held at a lower temperature (33° C.) and at a lower *p*H than is conventional. The Sheffield viruses in general conform to these criteria, and in fact no cold viruses were isolated by routine diagnostic methods. On the other hand, respiratory viruses belonging to other groups—adenoviruses, influenza, and others—grew quite well under "common cold conditions" as well as in conventional cultures, so they were not missed in the Sheffield tests. Only one of Hobson and Schild's viruses was in the M.K. group, and this was serologically distinct from the Salisbury prototype M.K. strain as well as from all the H.E.K. viruses. Whether or not these latter fall into several serological types cannot yet be said, since they grow only to low titre and to prepare antisera is therefore a slow and laborious business.

Experiments in volunteers and comparisons of samples of acute and convalescent serum from cold sufferers all join to support the idea that the agents under study are indeed causing the colds. The authors are cautious in assessing their quantitative importance as causes of colds and state that further work will be directed towards settling this question. They report one new finding of practical importance. Their M.K. strain and one from Salisbury can be propagated and produce cell destruction in one continuing line of cells derived from a human cancer, the H.E.pII line. This finding should prove practically useful, since monkey-kidney tissue-cultures are apt to be bedevilled by extraneous viruses of simian origin.

[1] Tyrrell, D. A. J., Bynoe, M. L., Hitchcock, G., Pereira, H. G., and Andrewes, C. H., *Lancet* 1960, 1, 235. See also leading article in *Brit. med. J.*, 1960, 1, 334.

URINARY RETENTION IN THE FEMALE

Retention of urine in the female occasionally poses a problem for the doctor. It is most often seen in labour or as an aftermath to a pelvic operation or childbirth. It is then so routinely looked for and excluded by nurse as well as doctor that it is very uncommon for it to reach the stage where it is masked by the symptom of overflow incontinence. At one time domestic remedies were persevered with to an extreme in the hope of avoiding catheterization, with its risk of introducing infection. Privacy and the use of a commode instead of a bedpan sometimes solve the problem, but running the tap usually has more effect on the mechanism of micturition in the attendant than in the patient. Now that retention is considered more likely than a properly performed catheterization to encourage infection, resort is usually made to the catheter if urine is not passed within eight to ten hours of pelvic operation or labour. As a rule there is no subsequent difficulty, but if the disability persists or recurs it is advisable to insert a catheter and allow the urine to drain continuously for about 48 hours.

Less commonly retention is due to a lesion in the nervous system or to a mass in the pelvis. Neurological disorders such as multiple sclerosis, tabes dorsalis, and lesions of the cord should be considered, but more often the cause becomes apparent on pelvic examination, when a large mass is felt which produces retention by disturbing the urethro-vesical junction. An impacted retroverted gravid uterus or a fibroid (particularly if cervical) is more likely to be encountered than an ovarian tumour, pelvic abscess, or haematocolpos. In

such cases the underlying condition requires treatment, but the decompression of the bladder should not be too rapid.

It has long been recognized that psychical as well as physical causes may precipitate retention. The older textbooks give much prominence to hysteria as a possible underlying cause, and the experienced gynaecologist is well aware of this possibility. Indeed, when troublesome retention of urine follows a hysterectomy, the surgeon may eventually be forced to the conclusion that the symptoms on account of which he performed the operation, as well as the subsequent retention, are all psychogenic. On page 1422 of this issue of the *Journal* Dr. S. J. Knox describes an extreme example in which psychogenic retention of urine after childbirth resulted in hydronephrosis and renal damage. His warning that intractable cases of retention without demonstrable organic cause warrant psychiatric assessment before surgical procedures are initiated is a timely one, because if the retention is found to have a psychical basis it is likely to be cured if the patient can be helped to become adjusted to her emotional problems.

CHILDREN IN TROUBLE

The report[1] of the Ingleby Committee on Children and Young Persons, appointed by the Home Secretary in 1956, has now been published. The British Medical Association was one of the bodies which pressed the Government to inquire into the operation of existing social services, "particularly from the point of view of preventive work to support and strengthen the family unit,"[2] and it is gratifying to see that the Ingleby Committee has adopted a number of the recommendations made by representatives of the B.M.A. in evidence. The report is both broad in scope and detailed in application. The problem of dealing with misbehaviour by and cruelty to young children has been exhaustively treated: unfortunately the Committee's terms of reference excluded any research into the causes of juvenile delinquency and of cruelty to children, but its report, however, makes the assumption that the state of the family is the key to most problems, and recommends that all efforts be made to discover families that are in need of help and advice before serious trouble arises. The family doctor is in a particularly good position to play a part in this process.

The most striking of the recommendations are those which urge the raising of the age of criminal responsibility from 8 to 12 years old, and the abolition of the rebuttable presumption in common law that children under the age of 14 are *doli incapax*. Under the present law, to obtain a conviction against such a child the prosecution must show that the child understands the difference between right and wrong: hence no punishment or treatment can be prescribed for children who do not understand this difference, although their need is clearly great. A new procedure is recommended for dealing with children under the age of 12 and with those now said to be "in need of care and protection." All such children should be brought to court as being "in need of protection or discipline," and should be subject to an order of detention in a remand home or attendance at an attendance centre, as well as the orders at present available in "care and protection" cases. The compulsory attendance of parents at the trial of their children is recommended. This new procedure has the great advantage that a child under 12 cannot start a "criminal record" by appearance in a juvenile court, but it does give rise to fears of "grandmotherly government" by local authorities, despite the restatement of the present basic principle that State intervention should be dependent upon proof of certain specifically defined allegations. These fears can only be effectively alleviated by a high standard of wisdom and restraint in the administration of the law. The Committee's report makes recommendations about the training and supervision of magistrates.

The Committee's recommendations on punishment do not go beyond a restatement of previously accepted principles and a considerable tidying-up of certain difficulties and anomalies revealed in evidence. The question of corporal punishment is not treated in the report beyond a mention that this is now a matter of separate inquiry by the Advisory Council on the Treatment of Offenders.

The Committee found that the social work of local authorities was much hampered by inter-service rivalries, so that the available resources were not brought to bear with maximum effect. The report divides such work into three stages—detection of families at risk, investigation and diagnosis, and treatment. If all detected cases were immediately referred to a special independent unit within the local authority (a "family advice centre") which would undertake the second stage, this unit could then allocate the case to the most effective department for treatment.

The report recommends that the power to bring proceedings in "care and protection" cases and in the new "protection or discipline" cases shall be vested solely in local authorities, and that the National Society for the Prevention of Cruelty to Children should lose their present powers in this respect. One member of the Committee regrets that this recommendation, vitally affecting the work of the N.S.P.C.C., was made without recalling the Society's witnesses to discuss the matter. However, the N.S.P.C.C. will still be able to bring proceedings in cases of cruelty. Of the recommendations concerning cruelty to children, the most important are that it should be made clear that to cause mental suffering falling short of mental derangement is to be an offence; and that in cases of cruelty to children more attention should be paid to the rehabilitation of the parents. It is to be hoped that the broad scope and the detail of this report will not delay speedy action upon its recommendations.

[1] Home Office. *Report of the Committee on Children and Young Persons*, 1960. H.M.S.O., London. Price 8s. net.

[2] *Cruelty to and Neglect of Children.* Report of a Joint Committee of the British Medical Association and the Magistrates' Association, 1956, B.M.A. House, London W.C.1.

W.H.O. IN THE CONGO

Developments in the Congo present one baffling situation after another to the United Nations, but in one direction at least the work of O.N.U.C. (Organisation des Nations Unies au Congo) is making welcome progress. Reporting last month to the Executive Board of the World Health Organization, Dr. M. G. Candau, its director-general, said that the Congo's health services had broken down completely when independence came, and that W.H.O. had therefore agreed to assist the "crash operation" of the United Nations in the Congo. Within a week 28 members of the staff of W.H.O. were in the country, and 25 national Red Cross organizations had provided 28 medical teams to work there. As a result of this immediate aid a number of hospitals were soon able to start functioning again, in the interior as well as in the big cities. Since then further medical help has arrived, and at each of the provincial capitals, except Katanga, W.H.O. has provided a public health adviser, a public health engineer, and a mobile epidemiological team. Dr. J. S. McKenzie Pollock, who has just relinquished the post of senior W.H.O. adviser in the Congo, recently enumerated the major dangers to health as smallpox, typhoid, and other enteric diseases, malaria, filariasis, yellow fever, sleeping sickness, leprosy, and tuberculosis; and a further urgent need was to confine plague within its endemic areas. We report elsewhere (p. 1462) an increase in the number of cases of smallpox in that part of Northern Rhodesia which borders the Katanga province of the Congo.

Dr. Candau was also able to report to his Executive Board that a group of 130 doctors and technicians were being engaged by W.H.O. to work for the Congolese Government, and that these temporary engagements would soon be increased to 400 or 500. But the complete lack of Congolese doctors, he thought, would mean another 12 to 15 years would have to pass before the health services in the Congo regained the place they had reached in 1959. Only two Congolese medical students were expected to graduate from Lovanium University, Leopoldville, in 1961, and even by 1965 there could not be more than 19 graduates. In an attempt to meet long-term needs W.H.O. had asked the university to enlarge its medical school and accept 30 to 40 students a year instead of 4 or 5. If this could be done W.H.O. would provide 9 professors for the school. W.H.O. had also offered fellowships to about 60 of the 138 medical assistants trained under the Belgian system, and a number of French universities had each accepted about 12 of these as students for a medical degree. Fellowships had also been given to seven young Congolese students with suitable educational attainments to enable them to follow the regular medical curriculum at Lyons or Geneva.

These notable efforts by W.H.O. will go only a small way to meet an enormous need, but they are at least an encouraging start and deserve success. But, as Dr. Candau emphasized, much depends on the political stability of the Congo. If that can be assured, he felt that there was no major health problem that could not be solved.

SUBJECT OF THE YEAR

Last year a number of Divisions of the B.M.A., and study groups within Divisions, discussed and reported on a subject of medico-social importance, adolescence, and in their deliberations they came to some useful conclusions.[1] The Council of the B.M.A. has decided to repeat this experiment and has chosen health education as the subject of the year. A steering committee has been appointed, with Sir Allen Daley as chairman, to give general guidance to Divisions and study groups wishing to tackle this subject, and to receive and collate the resulting reports. A useful leaflet has been prepared, outlining procedure, enumerating the general questions to which it is hoped Divisions will address themselves, and suggesting several topics — including, among others, nutrition, sex education, and accidents—for particular study.

There are many ways of trying to educate the public about health, and innumerable sources from which the public can gain information about health or disease—ranging from such periodicals as *Family Doctor*, published by the B.M.A., and *Better Health*, published by the Central Council for Health Education, to advertisements for patent medicines in the press or on I.T.V. The proposition that "dissemination of medical knowledge by means of television, radio, and the press does more harm than good to the health of the population" was debated at the Annual Meeting of the B.M.A. in Torquay a few months ago,[2] and the difference of opinion within the profession itself was seen from the result: 44 voted against the motion and 43 for it. It is fitting, therefore, that doctors should try to get clear in their own minds what they mean by health education so that they can answer the first of the general questions proffered by the steering committee: "Are doctors, by virtue of their medical training, qualified to appreciate the need for and to undertake health education?" Most will agree with Sir Allen Daley's words in his introduction to the steering committee's leaflet: "What is needed is to ensure that the right information is provided for the public at the right time and in the right way." If the Divisions and study groups can define what is "right" in this context they will have performed a most useful service.

The half-yearly indexes to Volume 1 of the *Journal* and *Supplement* for 1960 are now being dispatched. Members who have not previously asked for the indexes to be sent regularly to them can obtain copies, post free, from the Publishing Manager, B.M.A. House, Tavistock Square, London W.C.1.

[1] See leading article. *Brit. med. J.*, 1960, 2, 281.
[2] *Brit. med. J.*, 1960, 2, 48.

A PRESCRIPTION FOR THE REDUCTION OF PRESCRIBING COSTS

A THREE-MONTHS ASSESSMENT OF SERVICES RENDERED IN GENERAL PRACTICE

BY

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Among the more important and interesting words penned by various authorities during the past decade are these: "The Douglas Committee has seen how some doctors with persistently high costs . . . whose actions must have a serious inflationary effect on the costs of doctors anxious to retain their patients, go for years without any serious attempt made to investigate their costs" and recommends "that the Secretary of State should automatically require a panel to investigate the prescribing costs of any doctors whose costs exceed, for two consecutive issues of prescribing statistics, a given percentage above the area average, except where an investigation and formal report has been made by the Local Medical Committee on the basis of the first set." The Committee adds: "It seems to us that the most suitable percentage above the area average to be taken for this purpose should be 50%."

The prescribing costs for this practice (Table I) have, on occasion, been criticized. Our inability to conform to averages during 1955 obliged the local medical committee to send, on December 27, 1955, a courteous note suggesting that we try a little more conscientiously to economize.

Despite our best efforts, however, in December, 1959, we were invited to an interview with the committee in person. Various points emerged during the meeting, which was conducted in a courteous fashion by the chairman, and on balance the discussion was both interesting—to ourselves at least—and eventually profitable to others in that we were stimulated into analysing our efforts to play the physician during these financially stringent times and to see wherein we were among the "outsiders."

Before that, however, on January 11, 1960, we received a note from the secretary of the local medical committee which stated: "My committee is of the opinion that there has been excessive prescribing in your case. It considers that you have genuinely been sincere in your prescribing and that the cause of the excess is mainly due to excessive frequency in prescribing. My committee hopes that you will be able to reduce your costs and recommend that no action be taken meantime. Your costs will be kept under review."

This letter raises one obvious point of basic public interest. Of course we were sometimes "prescribing excessively," but only *in regard to average figures presented and according to the criteria laid down by the Douglas Committee.* More important, it seemed to us, was this further question: *Were we prescribing excessively in regard to what our patients required?* Therein lay the rub.

Maintenance Treatment

Other matters of moment had also emerged during the interview when, in general conversation, the following opinions were expressed. (1) "If patients are encouraged to come to the surgery, of course there will be a high proportion of 'maintenance' prescriptions issued because people do not like going away without a script"; and (2) in reply to the suggestion of G. B. M. that perhaps 50% of all patients seen at any clinic were present because of a need for "maintenance therapy," it was stated that this was a "shockingly high figure." But the further question arises: Is it?

The following opinions were also expressed by us: (1) that health nowadays costs money and that more and more people will, in the future, require maintenance treatment during their middle years in order to prolong life complicated by hypertension or other morbid processes; (2) that more and more people will require maintenance treatment during old age because of geriatric and other problems arising from increasing longevity; (3) that more and more active treatment in younger age-groups is now needed and will continue to be needed to reduce the acute period of many illnesses, to shorten convalescence, and to cure or maintain people who would have died in the past and who still do die in many other countries—perhaps sometimes even in

TABLE I.—*Prescribing Costs received May 3, 1955, to May 31, 1960*

	Sept. 1954	Dec. '54	Apr. '55	Nov. '55	Feb. '56	June '56	Nov. '56	Apr. '57	Aug. '57	Nov. '57	March '58	July '58	Dec. '58	March '59	June '59	Oct. '59
National average cost Form E.C.10	8/2½	7/9½	7/9½	7/10	7/10½	8/5½	8/6½	8/10½	7/0½	7,0½	7/3	7/8½	7/8	7/6½	7/7½	7/8½
Average cost per form of all doctors practising in area	7/9½	7/7½	7/7	7/7	7/9	8/2½	8/5	8/8	7/1½	7 0½	7'6½	7/11½	8 0½	7'10½	7'11½	7/11
Cost A.M.	9/5	9/7	8/0½	7'2	—	—	7'8½	8/5½	7/1½	6 7½	7/11½	7/11½	8'8½	8.7½	8'7½	8/3½
Cost G.B.M.	11 1½	10/0½	8 5½	7 5½	8'8½	8'2½	8 5½	7 8½	Nil	8 2½	8'8½	Nil	8 5½	—	8'9½	8'1½
Cost A.T.	Nil	Nil	Nil	Nil	Nil	Nil	Nil	Nil	,,	Nil	Nil	,,	8.8½	8/10	7/11½	7/2½
National average cost per patient	1/10½	2/1	2/0	2/1½	2/4½	2/0	2/4½	2/3½	2/1½	2/6½	2/7½	2/3½	2/11½	3/1	2/7	2/10½
Average cost per patient of all doctors practising in area	1/9½	2/0½	1/11½	2/0½	2/5	1/11½	2'4	2/3½	2'1½	2'6½	2'9	2/4½	3/2	3'5½	2/8	3'0½
Cost A.M.	2'10	3 1½	2 4½	2 2½	—	—	3 1½	2 8½	2 9½	3 4	3 9½	3 1½	5'0½	5 6½	3 10½	4 1
Cost G.B.M.	2 10	3 1½	2 4½	2 2½	3 4	2'5½	3 1½	2 8½	Nil	3 4	3 9½	Nil	5 0½	—	3 10½	4'1
Cost A.T.	Nil	Nil	Nil	Nil	Nil	Nil	Nil	Nil	,,	Nil	Nil	,,	5,0½	5 6½	3/10½	4/1
Total No. of patients on list	3,298	3,434	3,434	3,565	3,671	3,779	3,779	3,897	3,971	3,971	4,075	4,142	4,142	4.243	4,243	4,281
Month when costing figures were received	May 1955	Sept. 1955	Nov. 1955	July 1956	Feb. 1957	June 1957	Nov. 1957	March 1958	July 1958	Nov. 1958	March 1959	May 1959	Sept. 1959	Dec. 1959	Feb. 1960	May 1960
National average forms issued per patient									0·304	0·357	0·356	0·286	0·376	0·398	0·331	0·368
Area average No. of forms issued per patient									0·293	0·350	0·356	0·295	0·387	0·428	0·329	0·375
Forms issued per patient A.M.									0·394	0·471	0·464	0·390	0·585	0·635	0·459	0·529
Forms issued per patient G.B.M.									0 394	0·471	0·464	0·390	0·585	0 635	0·459	0·529
Forms issued per patient A.T.									Nil	Nil	Nil	Nil	0·585	0·635	0·459	0·529

Britain. (4) It was also suggested that if every patient needing maintenance therapy did, in fact, receive what was necessary—for example, all chronic bronchitics and arthritics who might be benefited by tetracycline or corticosteroids—the national and area averages would rise so abruptly that a new monetary approach would be forced upon the Government to meet costs.

Implicit in this was the suggestion that the present governmental disciplinary actions and veiled threats about mayhem being cast upon all who "over-prescribed" did lead to some patients at least being denied drugs of high price which they needed, and that to some extent, therefore, the Health Service must be second rate. In fact, one of us remarked: "The Government's attitude seems to be: let us accept a second-rate service which is financially possible rather than a first-rate one which we cannot afford without either raising taxation or charging patients some fee for every service as is already done in Australia under a Liberal administration."

We therefore set out to discover from our practice: (*a*) how many patients required essential maintenance therapy of some kind; (*b*) into what categories of illness these patients fell; (*c*) how many "acute" prescriptions were ordered and how many "maintenance"; (*d*) what patients could have treatment altered without suffering; and (*e*) how could we evolve a system whereby all maintenance patients could be studied by a neutral assessor should that be desirable.

With these considerations in mind, we began a three-months study of our work. During this time we kept a register of all maintenance patients, together with dates of attendance and a statistical break-down of all such cases into the categories of illness shown below.

Furthermore, all our cases were divided into: (1) maintenance cases seen at home; (2) maintenance cases seen at our clinics; (3) acute cases seen at home; and (4) acute cases dealt with at our clinics.

Finally, a record was kept of all patients seen who did not require any service or prescription other than general advice or a certificate.

We defined a "maintenance patient" as one who required continued treatment for more than six months. We included all pregnancies, whether normal or otherwise, because of their continued need for minerals and vitamins during a prolonged period.

It did not seem necessary for the purpose of this work to divide acute cases into groups. Maintenance cases, however, were broken down into: (1) Psychoneuroses, anxiety states, and tension. (2) Psychoses. (3) Hypertension. (4) Coronary artery disease. (5) Other cardiac disease. (6) Peptic ulcer. (7) Chronic rheumatic diseases. (8) Follow-up of rheumatic fever. (9) Chronic bronchitis, emphysema, and asthma. (10) Tuberculosis in any manifestation. (11) Peripheral vascular disease. (12) Cerebral vascular disease. (13) Diabetes. (14) Myxoedema and other endocrine disturbances. (15) Chronic blood diseases. (16) Malignancy of all types. (17) Pregnancy, whether normal or otherwise. (18) Unclassified (including such things as chronic skin problems, glaucoma, persistent otorrhoea, constipation, and the management of those "sickness-prone" persons who continually present with recurring minor health problems).

In correlating our results we have listed our figures in Table VI in order of frequency, and it is interesting to note the relative incidence of various important disease processes during our 13-weeks practice survey dating from January 18 to April 16, 1960.

Our analysis also continues the work covered by our practice review (Mair and Mair, 1959) and again checks upon the relative proportions of domiciliary and clinic services, number of services rendered, and proportion of practice patients served.

Finally, we have been able to discover how many patients suffered from multiple complaints during the period of study.

Before breaking our figures down further it may be useful to note the total number of services rendered (Table II).

TABLE II.—*Services Rendered During 13-Weeks Assessment*

Total No. of services demanded	6,722
No. of consultations during which no script was given	2 146 (31·92%)
Total No. of scripts given	5,999
No. of consultations involving the issue of one or more scripts	4,576 (68·08%)

We made a snap estimate at the local medical committee interview that approximately 50% of all cases seen during any clinic fell into the maintenance category, and our later investigations proved that this guess was not so very far out. Indeed, it remained fairly accurate even when considering these patients visited at home (Table III).

TABLE III.—*Relative Proportions of Acute and Maintenance Cases*

Total No. of patients seen during clinics	4,701
" " " acute "other" cases	2,610
" " " maintenance patients	2,091 (44·47%)
" " " patients seen at home	2,021
" " " acute "other" cases	1,272
" " " maintenance patients	749 (37·06%)

There is no reason to believe that the proportion of chronic sick in our own practice is larger than in that of others. The area which we serve is prosperous and compact, well housed, and with nearly full employment. It has even been described as Scotland's "boom town." We do not seek to create work. Even so, a large proportion of our entire practice seems to belong to the chronic-sick group and to be on maintenance therapy (Table IV). These figures give only the total number of

TABLE IV.—*Proportion of Practice on Maintenance Therapy*

Total No. of patients on our list as at April 1, 1960	4,316
" " " maintenance patients seen between January 18 and April 16, 1960	856 (19·83%)

patients falling into the maintenance category, but the total number of services given to this group is socially, economically, and statistically significant (Table V).

TABLE V.—*Services Rendered to Maintenance Patients*

Total No. of maintenance cases	856
" " " services rendered to 856 maintenance patients cases during 13-weeks period under review	2,840
Total scripts given to 856 maintenance patients during 13-weeks period under review	3,485
No. of attendances per maintenance patient per quarter annum	3.317
No. of scripts given per maintenance patient per quarter annum	4.071

Conditions Requiring Maintenance Treatment

The treatment of our maintenance patients is obviously of first importance to them, to our relations with the "prescribing authorities" in the broadest sense of the word, and to our own consciences. It follows that, bearing in mind our duty as citizens to be judicious in the expenditure of public funds and our other duty to give the best possible treatment to our patients, we

are also obliged to ask of ourselves how can the numbers of chronic sick be reduced and into what groups they fall. The resulting breakdown into categories is given in Table VI.

TABLE VI.—*Conditions Requiring Maintenance Therapy*

Condition	No. of Cases	No. of Scripts
Psychoneurotics, anxiety states, and tension	229	815
Peptic ulcer	102	397
Unclassified	98	606
Chronic rheumatic diseases	77	233
Hypertension	65	305
Chronic bronchitis and/or emphysema	51	295
Endocrine disturbances, including myxoedema	45	87
Coronary artery disease of the heart	41	160
Management of pregnancy	29	92
Peripheral vascular disease	19	66
Cerebral ,, ,,	19	53
Chronic blood diseases	19	60
Diabetes	16	64
Cardiac disease, excluding "coronaries"	15	106
Tuberculosis of all varieties	8	29
Malignancy ,, ,, ,,	8	33
Rheumatic fever follow-up	8	63
Psychoses	7	23
Total	856	3,485

As already explained, a register of all cases falling into these groups was kept during the 13-weeks period under review together with a note of each attendance. Adequate records are also kept of all our cases, and these reports are available.

One group is immediately obvious. No fewer than 229 patients needed help because of emotional problems, and 815 scripts were required to serve their essential needs. We shall all be grateful to anyone who may be able to advise us how such patients may otherwise be managed. So far as we can see, the only alternative is never to give them anything but advice to rely upon their own moral resources, to study the world's philosophies, and to turn to Jung in his final judgment that cure can be effected only after spiritual conversion to one of the religions of Light. But should this treatment fail, doctors who adopt it may have to face a personal emotional conflict in having failed to give tranquillizers or sedatives and finding they have fallen down in their prime duty to those who seek assistance.

But this group does not cover all cases which are due to tension. One must add those suffering from the three stress diseases—hypertension, coronary artery disease, and peptic ulceration. The grand total of stressed patients then rises to 437, or 51.05% of our chronic sick and 10.12% of our entire practice. Nor does that include all, since those suffering from certain skin lesions and the like have been excluded.

There is, however, a further complication in multiple complaints (Table VII). One patient, costly to the

TABLE VII.—*Number of Patients Suffering Simultaneously from More than One Disease Process*

No. of patients on our list	4,316
,, suffering from two chronic conditions	111
,, ,, ,, three ,, ,,	14
,, ,, ,, four ,, ,,	3

taxpayer, who falls into this last group suffers from hypertension, coronary artery disease associated with an infarct, advanced painful rheumatoid arthritis, and the stress of anxiety neurosis. She has lived for five years with the aid of increasing doses of "raudixin," "mycardol," varieties of aspirin or codeine, and "nembutal" at night (none very costly but considerable quantities required). She is typical of many others who are dependent on drugs.

Some Questions Answered

We have already explained that this paper was prompted by questions posed during our interview with the local medical committee, and it is now possible to answer certain of them with some assurance.

1. When patients come to a clinic prescriptions need not necessarily follow, because it has been shown that no less than 31.92% of all consultations involved only advice or reassurance and that no script was issued.

2. The comment that 50% was a "shockingly high" figure for maintenance patients during any clinic is, of course, debatable. But the fact is that 44.47% of all clinic cases and 37.06% of all domiciliary consultations involved exclusively the management of long-term problems, either physical or emotional, and were linked to the use of one or more scripts. We also believe that study of our register will prove that none of these people could, without disturbing progress, comfort, or expectation of life, have been denied anything which they were given and are "chronic" in the sense that "cure" is at present impossible.

It is our hope that the prescribing authorities will later co-operate in determining what proportion of our total expenses has been due, during the period of study, to the treatment of maintenance patients and enable us to present our findings in a later paper next year.

We believe, however, that a study of our case records and "maintenance register" will also prove that our earlier contention is correct—namely, that quality health nowadays does cost money. We further believe that it will cost increasingly large sums of money as time goes on and that more and more people will fall into the "maintenance category" as new drugs become available for the management of neoplasm, leukaemia, hypotension, psychoses, and so on. We also believe that the peculiar nature of our alleged civilization will increase stress throughout the foreseeable future until our relatively modest 10% total of stressed persons will rise to something nearer 50% of all in the country as a whole.

Good treatment nowadays does cost money, and there is no reason to believe that it will cost any less as time goes on. But already we note that a considerable number of persons joining our lists after removal to this town from other areas have not been given treatments which they often require. We have also noted that few arrive with any worth-while case notes whatsoever. And to continue this line of argument we know, from discussion with other doctors and with various patients, that important drugs have been, still are, and probably will continue to be denied to a proportion of people. Anxiety to maintain low average prescribing costs must largely be responsible for this.

However, the law is the true embodiment of everything which is excellent, and it is the duty of every citizen to observe the law both in letter and in spirit. Moreover, the title of this paper is "A Prescription for the Reduction of Prescribing Costs."

On the basis of the above study the prescription would appear to be:

1. Treat cases of emotional tension with advice, reassurance, and refer to marriage-guidance clinics, priests of religion, or to the study of selected books available at no cost within public libraries. Advise them to fortify their spiritual and moral character along these lines and rest one's case for denial of

tranquillizers upon the fact that they must "help themselves," put their own shoulder to the wheel, and count their blessings, etc. (or any other cliché which may come to mind).

2. Refer all acute cases to hospitals wherever possible.

3. Cut out the two- or three-year follow-up treatment of rheumatic fever with daily penicillin and refer relapses to hospital.

4. Never start any patient on an expensive drug with long-term implications lest it help him and he demands more and more and more throughout the years in order to keep at his work, and to enjoy a better general sense of well-being and an increased expectation of life. This, of course, applies especially to those with chronic bronchitis or arthritis and the giving of tetracycline, long-acting sulphonamides, and the corticosteroids. But it also applies to those with recurring deficiency anaemias, migraine, ulcerative colitis, and many other conditions. However, if every doctor in the country were to do the opposite and treat more and more cases at home, give the best therapy to all who require it, and sedate those who are emotionally disturbed, then both area and national averages for prescribing costs would rise very abruptly indeed.

The sequelae would probably provoke a need for major reassessment of the whole question of treatment under the Health Service, and we miss our guess if matters would stop short of yet one more Royal Commission which, if it did its work without prejudice, would end in a new fiscal approach to disease which might have far-reaching social and political effects.

Summary

Prescribing costs for a five-year period are listed.

Reasons for engaging upon a detailed study of use and abuse of scripts are presented.

Analysis of all work done over a 13-weeks period is listed in a series of tables which show, among other things, that 31.92% of all consultations required no prescription but that 44.47% of all "surgery" cases and 37.06% of all domiciliary consultations involved the management of "maintenance" problems.

The nature of these maintenance cases is considered and opinions are expressed in the light of the findings.

REFERENCE

Mair, A., and Mair, G. B. (1959). *Brit. med. J.*, 2, Suppl., p. 281.

The European Information Centre for Food Irradiation has been initiated and sponsored by the European Productivity Agency (E.P.A.) of the Organization for European Economic Co-operation (O.E.E.C.) on the recommendation of the Committee of Deputies of the O.E.E.C. Ministerial Committee for Agriculture and Food. The functions of the centre, at the National Institute of Nuclear Science and Technology, Saclay, France, are to co-ordinate the work of scientists, food technologists, and governmental and industrial circles interested in food irradiation and to encourage closer international co-operation in this field. The centre has now issued a quarterly international news letter, *Food Irradiation*, and copies may be obtained from Mr. N. B. McMASTER (Ministry of Agriculture, Fisheries and Food, Great Westminster House, Horseferry Road, London S.W.1), who is the United Kingdom national correspondent.

SYMPOSIUM ON INFLUENZA

[FROM A SPECIAL CORRESPONDENT]

Experts from the United Kingdom, Norway, and the Netherlands met in London on October 19, under the chairmanship of Professor C. H. STUART-HARRIS to discuss the epidemiology, virology, pathology, clinical features, and prevention of influenza. The conference, which was sponsored by Messrs. Pfizer, Ltd., opened with an account by Professor G. BELYAVIN (University College Hospital) of the antigenic structure and composition of the influenza virus as revealed in recent studies with the electron microscope. Spherical forms of the virus were seen to have an outer shell surrounding a dense inner core, the total diameter of the whole being between 60 and 180 millimicrons. The outer shell was probably the "large component" in which resided the infectivity of the virus and its haemagglutinating property; it had several different antigens that could be grouped into those that were specific to the virus itself and others that were serologically related to the host cells. The structure of this circumferential material was complex, consisting of at least two layers, each no doubt having different antigenic characteristics. The inner core appeared to have a skein-like structure of helical threads, and was probably equivalent to the "small component" isolated in ultra-speed centrifuge studies; although it was antigenic and complement-fixing, it was relatively non-specific and was common to the various strains of the virus. Professor Belyavin went on to classify the various strains responsible for human influenza epidemics, including types A1 and A2, B(Lee) and B1, but he pointed out that by various methods an almost indefinite number of subdivisions could be identified.

Asian Influenza

Dr. J. C. McDONALD, of the Central Public Health Laboratory, Colindale, described the epidemiological information obtained as a result of the Asian influenza epidemic which started in the spring of 1957. At first school-children and their families suffered most. By the end of the autumn some 50% of children had been affected. Families that did not include schoolchildren tended to escape the infection. Previous immunity to influenza A had little if any protective effect, at least so far as complement-fixation tests could show. Although most cases were among schoolchildren, nearly all the deaths were among the elderly and debilitated. After the first wave of infection there was a secondary wave, later in the year, mostly in older people. In 1958–9 the influenza epidemic had been due to types A and B, most deaths being among those with type A infection. By April, 1959, about two-thirds of the population had neutralizing antibody to the Asian virus, and the proportion was no doubt larger now. Second attacks had been very rare, and the maintenance of antibody levels was not due to reinfection.

Emergence of Epidemic Strains

Dr. C. H. ANDREWES, F.R.S., from the National Institute for Medical Research, Mill Hill, discussed the relationship between epidemiological behaviour and the antigenic characters of the virus. He emphasized that whatever tests were used to define antigenicity they must be meaningful in relation to epidemiology. New strains appeared to turn up only in epidemics. Studies with experimentally induced antigenic variations (for example, by passing virus through partly immune animals) had not so far been as

helpful as expected. Concerning the origin of the Asian epidemic, Dr. Andrewes speculated on the possibility of animal reservoirs where the infection might have lain dormant until it emerged in 1957. All the big epidemics seemed to have started in Central Asia, but investigations were complicated by the fact that new antigens were continually appearing.

Dr. J. FRY, of Beckenham, described the clinical features of the illness as seen in general practice. The general practitioner had to bear the brunt of an influenza epidemic since most cases were treated at home. Although the clinical features were usually diagnostic, in atypical cases there was no practicable laboratory test that was of value.

Dr. Fry recommended that symptomatic treatment only should be employed unless there was evidence or danger of a secondary infection, when antibiotics should be given. In his own practice, in the 1950–1 influenza A outbreak, the proportion with serious respiratory complications was 20%, but in the 1957 outbreak only 3% were so affected.

Pathological Changes in Fatal Cases

Dr. J. F. Ph. HERS, from the University Medical Clinic at Leyden, Netherlands, gave a detailed account of the pathological changes seen in fatal cases, in particular those seen by fluorescent microscopy. By using labelled antibodies the virus antigens could be seen inside the affected cells. These studies have revealed severe damage to the epithelium of the respiratory tract, producing an epithelial "wound" through which secondary bacterial invasion might occur, particularly by pneumococci, *H. influenzae*, and pyogenic cocci. The most serious of these invaders was the *Staphylococcus aureus*, which caused fibrinopurulent bronchitis and, by aspiration, bronchopneumonia. In some cases true influenzal virus pneumonia could be demonstrated, with intense alveolar and vascular damage and secondary formation of hyaline membranes and alveolar hyperplasia.

Diagnostic problems were considered briefly by Dr. D. A. J. TYRRELL from the Common Cold Research Unit at Salisbury. The same virus might cause a wide spectrum of disease in different individuals, from none at all to fatal bronchopneumonia. In between epidemics clinical "influenza" might result from a number of other viruses such as E.C.H.O. 20 and 11, the enteroviruses, and the adenoviruses. Laboratory studies were too slow to be of diagnostic value in individual cases.

Clinical Aspects

Clinical aspects of influenza were further examined by Dr. N. C. OSWALD, of the Brompton Hospital, London. He found that the Asian epidemic hit pregnant women and diabetics especially. Influenza might cause death in four ways: (1) toxaemia, (2) tracheo-bronchial obstruction, (3) pulmonary oedema, and (4) uncontrolled bacterial infection. Toxaemia usually occurred in children or young adults: it required treatment with corticosteroids as well as antibiotics. Patients with asthma and bronchitis were perhaps especially liable to tracheo-bronchial obstruction of sufficient severity to require tracheostomy. In pulmonary oedema tracheostomy and aspiration, in addition to antibiotics, offered the only hope of saving the patient. Bacterial infections occurred if antibiotic therapy was given too late or in insufficient dosage. About 10% of the cases of influenzal pneumonia were caused by staphylococci, and the mortality at all ages was about 30%.

Influenza Vaccines

Dr. J. A. DUDGEON, of the Hospital for Sick Children, Great Ormond Street, discussed the selection of strains for influenza vaccines. He pointed out that antibodies had a limited opportunity to come in contact with the virus, which was never blood-borne as in poliomyelitis. Vaccines had the ability to protect provided the antigens included A and B and the most recent strain of epidemic Asian. Influenza A was responsible for major epidemics, B for localized outbreaks.

Professor C. H. STUART-HARRIS, from the Department of Medicine at Sheffield, gave an account of the difficulties of field trials of vaccines. First of all the population must be chosen very carefully from among those most likely to be attacked. Residential schools were satisfactory apart from the interference of holidays. Groups of Service men might seem to be suitable, but they were always being moved around and a minimum of six months' stability was needed. Control groups represented a major problem and should preferably be equally exposed to the infection. Ethical questions arose when there was evidence that important protection was being given to the vaccinated group. Reactions to vaccination were also a problem but not a major one: young children were most susceptible to febrile reactions, but pilot studies could be made to assess the incidence of such reactions. Finally, there was the difficulty of ascertaining the illness. Serological tests were feasible only for a residential population, but were not feasible for subjects who were at home. Isolation of the virus was the ideal test but put a tremendous burden on laboratory staff. Perhaps some method of randomly sampling the population at intervals was required.

Control of Epidemics

In the concluding paper Professor R. CRUICKSHANK, from Edinburgh, said that of the three methods of controlling epidemics—quarantine, air hygiene, and specific vaccination—the last appeared to be the most promising. The vaccine must be practicable, safe, and effective. It was important to avoid egg allergy with vaccines prepared by the chick-embryo method. The vaccine should be capable of causing at least a 50% reduction in the incidence of the disease. Professor Cruickshank did not think that the whole population needed to be vaccinated, and he would restrict it to the following groups: (1) doctors and nurses, (2) those operating public utilities such as transport, (3) highly specialized or "key" staff such as airline pilots or top executives, and (4) people at special risk because of diabetes, pregnancy, bronchitis, or heart disease.

IMMUNOLOGY IN THE RHEUMATIC DISEASES

[FROM A SPECIAL CORRESPONDENT]

A symposium on Immunology in the Rheumatic Diseases, sponsored by the Empire Rheumatism Council, was held on October 28 in the Apothecaries Hall, London. The chairman for the morning session was Dr. W. S. C. COPEMAN, and for the afternoon Professor J. R. SQUIRE.

Auto-immunity

The first paper was by Dr. L. E. GLYNN on auto-immunity. He drew attention to four factors mainly responsible for the recent upsurge in popularity of auto-immunity as a process of important pathogenic significance: firstly, the discovery that in many patients with acquired haemolytic anaemia circulating antibodies could be found with a specific affinity for defined antigens on the red cells of the same individual; secondly, the production of a variety of experimental lesions in animals by auto-immunization techniques; thirdly, the phenomenon of acquired

immunological tolerance demonstrated by Professor Medawar and his colleagues; and, fourthly, the presence in several of the rheumatic diseases of certain serological factors—for example, the L.E.-cell factor, with many of the properties of auto-antibodies. In considering the various ways in which auto-immunity could arise he advanced ten possible mechanisms. Dr. A. G. S. HILL then undertook a clinical review of immunological processes in pathogenesis. This was presented in the Socratic manner and with the somewhat misleading conclusion that the strongest evidence in favour of auto-immunity in the aetiology of rheumatoid arthritis was the absence of any other acceptable cause.

Dr. DEBORAH DONIACH presented the results of a combined study, from three centres, of the overlap of thyroid auto-immunity with the L.E. phenomenon and rheumatoid arthritis. Some overlap was found but not to a striking degree. Thus of 182 patients with Hashimoto's disease only 15 gave a positive test for antinuclear factor and none was positive by the L.E.-cell test. Conversely, although 23 of 55 cases of disseminated lupus and 4 out of 50 cases of rheumatoid arthritis contained antibodies to thyroglobulin these were only present to a low titre, similar to that found in 6 of 120 normal controls. Whereas no significant sex difference was observed in the incidence of these antibodies in any of the above diseases, in discoid lupus antibodies were found in 9 of 16 females but in none of the 8 males examined. Dr. I. M. ROITT reported that he had found no sex difference in the ease with which thyroiditis could be produced experimentally.

Complement and Immuno-conglutinin

Complement levels in rheumatoid arthritis and disseminated lupus erythematosus were discussed by Dr. H. ELLIS. He had used two different methods to estimate complement, haemolysis, and gel diffusion precipitation. Essentially similar results were obtained by both methods. These showed that in rheumatoid arthritis there was a significant rise in the level of complement, especially in the early stages: in disseminated lupus erythematosus there was a considerable fall. Mean levels in arbitrary units in control subjects and in patients with rheumatoid arthritis and disseminated lupus erythematosus were 112, 145, and 36 respectively. He therefore suggested that the level of complement could have diagnostic value.

The extensive work on immuno-conglutinin was reviewed by Dr. R. R. A. COOMBS. It was shown that this serum factor was best regarded as an auto-antibody to complement, but he stressed that this antibody was not directed against native complement but only against complement that has been altered by its reaction with an antigen–antibody complex. He further reported that, although the level of immuno-conglutinin was much raised both in rheumatoid arthritis and in rheumatic fever, this should not be taken as evidence of an infective aetiology, since the presence of any *in vivo* antigen-antibody reaction capable of fixing complement could stimulate the formation of immuno-conglutinin.

Dr. R. G. WHITE demonstrated that the histological appearance of the lymph nodes in rheumatoid arthritis was typical of a classical immune reaction obtained, for example, in a rabbit after injection of some foreign protein. By means of the fluorescent-antibody technique he was also able to show two types of cell-reaction associated with antibody-formation, firstly the development of plasma cells in the medullary cords and secondly foci of lymphopoiesis in the germinal centres.

Rheumatoid Factor

The complex story of the rheumatoid factor and its significance was dealt with by Dr. J. BALL and Dr. C. L. GREENBURY. In 2,000 apparently normal subjects Dr. Ball had found a positive sheep-cell test in about 5%. The incidence of positive reactors was higher in the relatives of reactors and there was also a positive correlation between the raised incidence in the relatives and the titre of the factor in the propositus. Since a significant proportion of those with rheumatoid arthritis developed a positive reaction only after the clinical onset of their disease, he suggested the possibility that the rheumatoid factor might appear as either an inherited or an acquired character. He did not feel able to draw any definite conclusions about the mechanisms underlying either the occurrence of rheumatoid type gamma-globulins or their particular relationship to certain rheumatic diseases. He did however conclude that these globulins included a group of proteins with a varying range of individual specificity in their reactions with other gamma-globulins. Dr. Greenbury's results, using rheumatoid sera or fractions labelled with ^{131}I, were also interpreted by him as indicating a heterogeneity of factors capable of reacting with sensitized cells. Dr. GLYNN, however, pointed out that the difference in behaviour of the rheumatoid factor towards heavily and lightly sensitized cells could as justifiably be interpreted as due to differences in the degree to which the sensitized antibody was unfolded in these two circumstances.

In an account of the histological evidence of antibody-production in rheumatoid arthritis, Dr. B. CRUICKSHANK pointed out that the majority of plasma cells gave reactions for neither 7S nor 18S gamma-globulin. Neither he nor any of the other participants could, however, suggest the nature of any other product of plasma-cell activity. An investigation by Dr. J. N. MCCORMICK of the distribution of the rheumatoid factor, utilizing heat-denatured, fluorescein-conjugated gamma-globulin as a histochemical reagent, was presented by Dr. A. G. S. HILL. Although the factor could by this means be readily detected in plasma cells, much of the globulin present in the germinal centres did not react positively with the test reagent. Dr. MCCORMICK, however, pointed out that this could be due to the presence of 7S gamma-globulin in those areas already specifically combined with rheumatoid factor.

Connective-tissue Antigens

Dr. D. G. SCOTT described a mixed staining technique for the study of connective-tissue antigens. This made use of an antiserum to renal glomeruli and another to synovial membrane. One was conjugated with fluorescein and the other with rhodamine. From the results of staining with a mixture of these two reagents three components of human connective tissue were differentiated. These were basement membrane, reticulin, and a fibrillar material found in the adventitia of vessels, in fibroblasts, and between some bundles of collagen fibres.

The reaction of the skin to injection of synovial fluid from rheumatoid joints was studied in Edinburgh some years ago. Dr. W. R. M. ALEXANDER reviewed these old results as well as more recent ones. Synovial fluid from some patients with rheumatoid arthritis when injected into other patients or controls produced a delayed type of skin reaction that persisted for up to five days. Donors rarely reacted, however, to injections of their own fluid. Synovial fluid from non-rheumatoid arthritis failed to elicit this reaction. The active principle was remarkably labile to heat and storage; it was intimately associated with gamma-globulin but was not identical with the rheumatoid factor.

Antinuclear Factor

The incidence and the nature of the antinuclear factor were discussed by Dr. D. M. WEIR. He had found the factor in almost every patient with disseminated lupus erythematosus, but also occasionally with some other diseases, especially of the "collagen" group. He had found, however, that in these other patients the factor often differed in many of its properties from that in disseminated lupus

erythematosus ; thus, in these other diseases it was often a macroglobulin, its titre was usually lower, and it was not always absorbable by calf-thymus nucleoprotein. He presented convincing evidence that it was an antibody to histone, as it existed when combined with deoxyribonucleic acid.

Dr. G. J. FRIOU drew attention to the poor antigenicity of nucleoprotein, from which he concluded that the presence of anti-nucleoprotein antibodies in disseminated lupus erythematosus was indicative of a fundamental change in immunological reactivity in that disease. His attempts to isolate the L.E. factor had up to now been frustrated by its extreme lability to fractionating agents. The L.E. factor was also discussed by Dr. W. HIJMANS. Despite a vast amount of work on the factor responsible for the phenomenon, he concluded that there was no evidence that it exerted any pathogenic effect. He had however observed that addition of the factor to chick-embryo fibroblasts in tissue culture produced a very few swollen nuclei somewhat resembling haematoxylin bodies.

The final paper, by Dr. E. J. HOLBOROW, dealt with the important problem of the antigenicity of polysaccharides and their possible role as auto-antigens. He drew particular attention to the conversion of non-antigenic polysaccharides to complete antigenicity by their absorption on to streptococci, and to the correlation between polymer size and antigenic potency.

BIOLOGICAL ENGINEERING SOCIETY

The first scientific meeting of the Biological Engineering Society was held on October 15 at the National Institute for Medical Research, Mill Hill. About 100 participants assembled in the morning to listen to a series of short papers, each describing a demonstration held during the afternoon. Sir CHARLES HARINGTON, F.R.S., director of the Institute, opened the proceedings by welcoming the Society, and in his address he drew a parallel between the state of biological engineering to-day and biochemistry half a century ago. Perhaps in the years to come a fusion of the two disciplines of biology and engineering might result in biological engineering becoming as acceptable as biochemistry to-day. In the meantime, advances in biological and medical science were very dependent upon advances in engineering and instrumentation, and the Society was making a valuable contribution by enabling biologists and engineers to work more closely together and to understand each other's points of view. Professor R. F. WOOLMER, president of the Society, replied.

Demonstrations

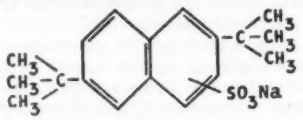
The demonstrations were chosen to represent a fair cross-section of the subjects which the Society hopes to cover in its activities, and were as follows: (1) Metallic implants in orthopaedic surgery (J. T. Scales). (2) A solid image microscope (R. L. Gregory). (3) Artificial voice appliances (R. V. Tait). (4) The Hendon prosthesis motor (B. Kinnear-Wilson). (5) The detection of radioactive zones from a gas-liquid chromatogram (A. T. James and E. A. Piper). (6) A study of the chemical structure of gas molecules by their electron affinity (J. E. Lovelock and N. L. Gregory). (7) Kinetic gas analysis (B. M. Wright). (8) High impedances without valves (H. S. Wolff). A number of demonstrations were also presented by research teams working at the Institute. These included exhibits entitled "A Time-event Digital Recorder," "Preparative and Analytical Chromatography," "Recording of Physiological Data on the Himalayan Scientific Expedition," "Estimation of Enzyme Activity of Single Cells," "Ideas and New Techniques," "A Precision Operating-table for Physiological Use," "A Multi-directional Radial Shaker," "Phantom Man for the Study of Ionizing Radiation Dosage."

To-day's Drugs

With the help of expert contributors we publish below notes on a selection of drugs in current use.

"Becantyl" (Horlicks)

Chemistry.—This drug is a derivative of naphthalene and is sodium 2-6 ditertiarybutylnaphthalene monosulphate, with the following structural formula:



It is a white, slightly hygroscopic powder, soluble in methanol and sparingly soluble in cold water.

Pharmacology.—The therapeutic action of becantyl is to depress coughing. The only experimental study of this action showed that the drug completely blocked coughing attacks in unanaesthetized dogs exposed to sulphuric acid aerosol. The intravenous dosage was 10–20 mg./kg. body weight. Since the drug did not block coughing induced in anaesthetized dogs by nasopharyngeal irritation and vagal-nerve stimulation, it is claimed that becantyl acts on peripheral nervous endings in the lungs and air passages and not on the central nervous system ; details of these latter experiments have not been given. Its action, if any, on respiratory tract secretion has not been studied.

Similar doses of becantyl did not depress breathing of anaesthetized dogs, and had no action on blood-pressure and heart-rate. Larger doses (up to 50 mg./kg.) caused respiratory stimulation, transient variations in blood-pressure and heart-rate, and weak peripheral vasodilatation.

The acute oral toxicity in rats was over 8–10 g./kg. of body weight for 50% mortality. Similar doses occasionally caused a late mortality (after 8–10 days) and late skin eruptions (after 1–4 weeks). Since these doses are about 1,000 times the recommended human daily dose, lethal toxicity must be virtually absent in man if interspecific comparisons are valid.

Therapy.—Several clinical trials have been reported. It is regrettable that they have not been adequately controlled, and that comparison with other drugs has not been investigated in detail. Based mainly on the assessment of physicians and patients, the reports agree that becantyl effectively relieves coughing due to a large number of conditions in adults, children, and infants. The dosage recommended is 30 mg. (as two tablets or 7 ml. of syrup) three or four times a day for adults ; 14 mg. (3.5 ml. syrup) for children 3–6 years old, and 14–30 mg. (3.5–7 ml. syrup) for children 7–15 years old, both three times a day.

Side-effects.—No serious side-effects have been reported. Minor gastric upsets have been recorded, and the bitter taste of the tablets makes the syrup more suitable for young children. In particular, respiratory depression, narcosis, and constipation do not seem to occur.

Summary.—Becantyl seems to be an effective antitussive drug without significant toxic effects, though its mode of action is not understood. It is a useful member of the range of drugs for treating cough, being especially worthy of trial in young children and the debilitated, and in patients for whom codeine, methadone, and similar antitussive drugs are contraindicated.

N.H.S. Basic Price.—10 fl. oz., 6s. 2d. ; 24 tabs., 2s. 11d.

The most noteworthy feature of the *Annual Report 1959* of the Tanganyika Health Services is the increased demand for hospital services. Compared with 1958 diseases diagnosed in in-patients rose by 3,485, an increase of 1.6%, while diagnoses in out-patients rose by 127,513, an increase of 8% on the 1958 figures, giving an overall increase in hospital usage of 7.4%.

Correspondence

Because of heavy pressure on our space, correspondents are asked to keep their letters short.

Service Overseas

SIR,—The letter from Dr. H. B. L. Russell (October 29, p. 1313) emphasizes more than ever the need for a central organization to promote and encourage service abroad by British doctors and the need for funds to help those who are prepared to work in countries which are short of doctors. The lack of such an organization has left Dr. Russell in ignorance of what is already being done. To give a few examples—Sims Travelling Professors and others from the Royal Colleges regularly visit Commonwealth countries, the Colonial Office sends visitors to the territories under its control, the University of Birmingham have agreed to sponsor the new medical school in the Central African Federation, and the Nuffield Foundation have provided the means for a few students from two English medical schools to spend part of their final year at medical schools in Africa.

It must be admitted that the seconding of staff either from the universities or the National Health Service has been on a disappointingly small scale and that those serving abroad are handicapped in obtaining senior posts in the National Health Service, but there is a tendency that the value of such service is becoming more widely appreciated by appointing committees.

Dr. Russell can be assured that some of our medical schools have a very active interest in the problems which he raises, but as they have no resources of their own for this purpose they are unable to take all the practical steps which they would like to put into effect. It is to be hoped that before long there will be a more co-ordinated effort to bring together and expand the sporadic efforts which are being made. If this is not done, others, as he says, are only too ready to step in both with men and money.—I am, etc.,

Department of Surgery,
University of Bristol. R. MILNES WALKER.

⁂ The subject of overseas appointments was discussed in an annotation last week (November 5, p. 1376).—ED., *B.M.J.*

SIR,—The letter from Dr. Hugh B. L. Russell (October 29, p. 1313) on British Medicine Overseas once again draws attention to an already much discussed subject which is causing concern to many who feel that British doctors have a responsibility to give other than material help to the so-called developing countries, especially to those with present or previous close links with Britain. The vast majority of those with such feelings are consultants, or those in established positions. One can hardly expect to find such feelings burning in the hearts of registrars whose thoughts are fully occupied with their own careers, especially when they have little or no evidence to suggest that a period overseas is an advantage to them in scaling the ladder to consultancy. Hence it is the consultants who must take the initiative, and take it personally rather than as an impersonal collective body.

Registrars are not likely to entrust their careers to impersonal official organizations, but they are usually prepared to place such trust in a consultant whose advice and opinion they respect. They are only likely to spend a period overseas if advised to do so by such a consultant and with his support. I feel, therefore, that consultants must interest themselves in their own specialist departments in overseas territories, and acquire information (personally if possible) about the country, the staff, the hospitals, and the living accommodation, as well as the medical facilities and opportunities, so as to give some general guidance on how a registrar might make maximal use of his stay. They must be prepared to visit the country themselves, and the registrar must have the strongest possible backing from them in the next step in his career on return. Furthermore, the consultant must maintain a liaison by his interest and help in the work which the registrar is doing overseas. The registrar will often need advice and support in matters of teaching, research, and eventual publication of his work. Most important also is the fact that only consultants can usually help registrars to obtain the money required.

Official bodies and organizations are not likely to be the most effective agents in inducing doctors to work overseas, but they can give very valuable and necessary help in providing (*a*) "ways and means," and (*b*) an information centre.

Dr. Russell is right in saying that the urge for security, as exemplified by the Welfare State, is a deterrent. The National Health Service has unfortunately made it more difficult to have a varied career in medicine to-day. The ladders to consultancy are too narrow, simulating the progress by seniority of a Civil Service. Registrars can only be expected to spend a year overseas, if it is accepted as a rung on the ladder. The best way to achieve this is by secondment; a registrar should be given study leave with pay, and return to his appointment in the same way that most of them go to the United States. Only under such conditions will our best registrars agree to go to the developing countries, and it is of vital importance that the best and not the second-best doctors are attracted there.

In spite of discussion meetings sponsored by many official bodies, practical achievements have almost all come from individual efforts. The association of the Hospital of Sick Children, Great Ormond Street, with Makerere College in Uganda, is the model of what can be done. Similar efforts are being made by other individuals and hospitals, but they require help with ways and means from the Royal Colleges, the B.M.A., the Commonwealth Office, and Research Foundations.—I am, etc.,

St John's Hospital for Diseases
of the Skin,
London W.C.2. C. D. CALNAN.

SIR,—The letter from Dr. Hugh Russell (October 29, p. 1313) warmed my heart, for what he says Professor W. C. Nixon and I have been writing about to you and preaching aloud for years. I do not think that it is the sense of adventure in modern medical youth that is lacking, but rather the fact, alas, that to-day so many are married inordinately young and have families below teen age. Such men, unless missionaries, will not, or dare not, risk insecurity, climatic and school problems, together with the possibility of missing a hospital or N.H.S. queue.

During the last 48 months I have been as far east as Hong Kong and as far west as San Francisco as guest surgeon or lecturer in almost all the countries between. This has enabled me to see ample proof of what Dr. Russell asserts, but I would emphasize that the standard of ethics and practical knowledge shown by many colleagues of foreign nationality in some countries was deplorably low. Indeed, so low that it was my opinion that many were animated, educated, and compelled to

action solely by the huge output of drug-houses and patent-medicine literature which flooded into their offices by every mail. Indeed, one felt pity for any problem medical or surgical case that fell into the hands of such professional detritus, for, although quantity may fill a needful and temporary gap among ignorant, indigenous people, it is real quality that pays dividends in the long run.

The suggestion that medical schools here should take active interest in embryo medical schools in distant countries is one (already partially adopted by another country) that cannot fail to appeal to every medical member of the Commonwealth, provided those initiating and developing these new schools are not forgotten, for only by an exchange of men and women, together with a change of heart in the administrators of the N.H.S., can we regain our prestige among former friends in less well placed lands. If that be achieved good will and trade must inevitably follow.—I am, etc.,

London W.1 V. B. GREEN-ARMYTAGE.

Congenital Deformity

SIR,—The articles by Mr. W. A. Crabbe (October 8, p. 1060) and Mr. William Hunter (October 15, p. 1124) illustrate the curious fragmentation of medical thinking at the present time. Mr. Crabbe writes of deformities of infants without considering the mechanics of pregnancy, and Mr. Hunter of mechanical abnormalities of the uterus without mentioning the effect of these on the babies they produce. The baby here illustrated

would interest them both. It emerged from one-half of a bicornuate uterus in a mother otherwise perfectly normal and healthy. The child is normal except for (*a*) double varus talipes; (*b*) one dislocated hip; (*c*) two dislocated knees; (*d*) "arthrogryposis" of both legs below the knee.

Now this syndrome is simply explicable upon the general theory of intrauterine forces, with special theories for particular conditions such as talipes, which I have tried to teach for many years.[1] These theories explain and bring into relation: talipes, as defined below; club-hands, defined similarly; congenital dislocation of the hip; congenital bends of bones (not pseudarthrosis); arthrogryposis affecting the lower limbs only; arthrogryposis affecting all four limbs; congenital postural scoliosis (idiopathic scoliosis[2]); the spina-bifida-hydrocephalus-Chiari-deformity syndrome (not simple spina-bifida); congenital ring constrictions (often described as amniotic bands)[3]; dimples over bony points; maternity pregnancy histories, too much or too little liquor; and uterine deformities such as bifid cavities.

The argument turns on the use of:

Imagination.—Working out the ways in which the mechanical relation between mother and foetus could go wrong. These are: (*a*) Malposition, wrong folding up of the foetus. (*b*) Increased mechanical pressure, with dysplasia of muscles and stiffening of joints analogous to that seen later in life after long-continued tight plastering. (*c*) Increased hydraulic pressure, with effects analogous to those occurring in papilloedema. (*d*) Penetration of amnion, with ring constrictions at site of penetration.

Definition.—I think it is worth defining a condition before discussing it. As Francis Bacon observed: "There arises from a bad and unapt formation of words a wonderful obstruction of mind." The word talipes is badly used in two ways, either too narrowly to mean only that misshaping unaptly called equinovarus, or too widely to mean any deformity of the foot, including those caused by spasticity and paralysis. I have proposed that the term should be confined to deformities of the feet or hands that *could* be produced by moulding. I am aware there are logical and etymological objections to this, but it is the best I can do.[4]

Observation.—If a few thousand deformities of the feet are observed it will be found that three regular forms occur repeatedly in different degrees: (*a*) Club-foot or equino-varus due to malposition. (*b*) Metatarsal varus due to malposition. (*c*) Metatarsal valgus due to increased mechanical pressure. In addition, there are an infinite number of irregular forms, associated with variations of position and pressure.

Analysis and Reasoning.—(*a*) Many children with moulding deformities are otherwise perfect specimens. This makes nonsense of the hypothesis of a toxic origin of talipes. Of course, if a child is completely misbegotten, its relations to its surroundings are apt to go wrong as well as its mentality, palate, or bowels. (*b*) The variety of mouldings makes nonsense of the hypothesis of arrest in foetal development. (*c*) Brockman's suggestion[5] that talipes is due to dislocation of the astragalo-scaphoid joint, and Keith's[6] that it is due to a patch of dysplasia, both mistake effect for cause. (*d*) Oddities such as blaming our simian ancestors because they turned their feet in are not worth discussing once the variety of mouldings is recognized.

Correlation of different conditions consistently found together. This was one of the favourite methods of John Hunter, and it is interesting to imagine what he would have said of the present refusal of orthopaedic surgeons to consider intrauterine mechanics, on the ground that these belong to another closed shop, that of the obstetricians. I select a few out of many: (*a*) In bilateral talipes one foot is always more deformed than the other—it is the one on the outside in the cross-legged malposition responsible. (*b*) Valgus feet always have weak leg muscles. (*c*) Valgus feet are frequently associated with congenital dislocation of the hip. (*d*) Varus feet, in my experience, are never associated with congenital dislocation of the hip unless the knees have been hyperextended. (*e*) When the baby shows signs of compression the mother has had a small and uncomfortable pregnancy. (*f*) In four-limbed arthrogryposis there is frequently a history of hydramnios, which suggests increased hydraulic pressure, which suggests venous obstructions, which suggests its well-known effects on tissues, cf. papilloedema. (*g*) In four-limbed arthrogryposis babies are frequently born with stiff extended hips, a position which could occur only in a uterine cavity larger than normal, hence a presumption of hydramnios. (*h*) Mutual deformities frequently occur—for example, a concavity on one foot fits a convexity on the other. (*i*) All mouldings of the feet and hands show a convexity on one surface corresponding to the concavity of the uterine wall. (*j*) Complicating deformities occur more frequently with valgus mouldings than with varus ones.

Discussion.—This could be so fruitful, and yet is so rare and difficult in our profession. I could wish we thought more like scientists and had less resemblance to theologians in our refusal to give a hearing to heresies.

Treatment.—The results of this provide a useful check of the correctness of the pathology on which it is founded. Mr. Crabbe mentions the use of one of my splints. If it is the hobble one for club-feet I hope he has not fallen into any of the commoner twelve errors in its manufacture and application which I once listed.[7]

—I am, etc.,

London W.1. DENIS BROWNE.

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Faecal Incontinence in Children

SIR,—To call "heads" or "tails" correctly six times out of seven is always an achievement, but particularly so in diagnosing the causes of faecal incontinence, as Drs. Marian Coekin and Douglas Gairdner (October 22, p. 1175) claim to have done. The mechanical aspects of this problem needed restating, and your contributors have done this neatly and clearly; possibly even too clearly, for their account gives an impression of over-simplification. I agree that physical factors are often important, but is it really so easy to distinguish between these and the emotional factors with which they are interwoven?

Under the heading of "mechanical factors" the authors attribute many cases to congenital constipation, but their use of this term is open to serious criticism. Case 5, for example, which is quoted as one of those leaving "no doubt of the existence of constipation as a congenital disorder," might reasonably be interpreted as typical of anal fissure. Then it is difficult to reconcile the statement that there is "often" a history of constipation in the first months of life with the figures given, which show that in three-quarters of the group no such history was obtained. Again, if so large a proportion of cases did originate as congenital constipation, would one expect such permanently good results from a brief period of medical treatment? As regards the psychological group, it provides food for thought that "nearly all these children showed obvious signs of emotional disorder," as compared with the mechanical group in which behaviour disorders were "conspicuous by their slightness." It seems so easy; but details about the methods used should have been given, to dispel any suspicions that the psychological assessment was superficial. Unfortunately, almost nothing is said about the parents; yet psychological assessment of children without an adequate knowledge of the parents' attitudes can be grossly misleading.

The authors remark rather defiantly that separation into somatic and psychic factors is unfashionable. Treatment by repeated bleeding is now unfashionable; and circumcision is becoming so, as Dr. Gairdner should well know. A decline in popularity may be due to advances in knowledge. In the disorders of complex humans living in a complex world the question, "Either . . . or . . . ?" may give misleading answers. A clear-cut approach to diagnosis, especially if it leads to a simple form of treatment, is always attractive; but it might satisfy the doctor more in the short term than the patient in the long. It would have been interesting to know what happened after several years to the patients in this series who were "cured." I suspect that the "heads *plus* tails" group would be much larger than in the authors' present assessment.—I am, etc.,

The Children's Hospital, Bristol 2. JOHN APLEY.

SIR,—The article by Drs. Marian Coekin and Douglas Gairdner (October 22, p. 1175) will be remembered for the descriptions of infants with constipation dating from soon after birth. Some of these are gems, but some of the conclusions drawn about the other cases are surprising. The authors rightly say that the physician has a duty to attempt to elucidate the main factors in each case of faecal incontinence. They ought to add that when his investigations are incomplete or inconclusive he must admit the main factors to be unknown, and they might have realized that ascribing faecal incontinence to constipation can be useful but as an aetiological conclusion is very unsatisfying.

They consider that in 36% of their cases psychological factors were mainly or partly responsible for the symptom of faecal incontinence and that 64% were due to mechanical causes. It is reasonable to conclude that when infrequent passage of hard stools had existed from birth a congenital (primary) inertia of the colon was present. But is it fair to say that such constipation from the first few weeks or months is "typical" when it was found in only 12 of the 44 cases—and to imply that all 44 were due to "primary inertia"? On their data as published it would have been fair to have concluded that in 27% the cause was mechanical (congenital primary inertia), in 36% psychological mainly or in part, and in 37% was unascertained, albeit associated with constipation (the origins of which do not appear to have been studied comprehensively).

It is too late in the twentieth century to be satisfied with explaining faecal incontinence by saying it is due to "constipation." Constipation (*O.E.D.*) is when the evacuations are stopped. If the evacuation of the colon contents is stopped there will be further absorption of water and the stools will become harder. Is the stoppage—the constipation—not sometimes an *active* retention from dislike of going to a smelly w.c.; the desire of a toddler to assert his independence or of an older boy to make a further gesture in a long-term quarrel between child and parent? Constipation, soiling, and encopresis are symptoms whose origins may be predominantly somatic or psychic, or due to a mixture of both. A series of patients, each of whom has been seen both by the general physician and by the psychiatrist, would provide a much better basis for a reliable estimate of the relative frequency of somatic and psychic factors as the main causes of this symptom, and many would say that a follow-up after "cure" is necessary before publishing. This paper purports to make such an estimate without adequate study of the cases either before or after treatment. What would be very useful would be a detailed study of the 12 cases with colonic inertia dating from birth or soon after, and it is very much to be hoped that Drs. Coekin and Gairdner will give us this.—I am, etc.,

Guy's Hospital, London S.E.1. RONALD MAC KEITH.

SIR,—I refer to the paper on faecal incontinence in children, by Drs. Marian Coekin and Douglas Gairdner (October 22, p. 1175). May I, through your columns, be allowed to correct certain erroneous assumptions made

by these authors in reference to my earlier work[1] with a similar series of children? Quite rightly, the authors differentiate between two main groups of cases—namely, those with constipation as a primary condition, in whom, if soiling occurs, it is of the overflow type; and those in whom soiling is the primary symptom. In this latter group psychogenic factors are acknowledged to play a predominant role, and, because of this, it was incorrectly assumed that I was dealing with this second group in my own series. In fact I was not.

I was indeed describing the so-called "mechanical" group of soilers, but whereas Drs. Coekin and Gairdner deny the operation of psychogenic factors in this group, except as a secondary development, my entire thesis was based on the demonstration that emotional factors play a primary aetiological role. Constipation certainly exists, and constitutional sluggishness of bowel action was also apparent in my own series of cases, but physiological influences alone did not produce the picture of "psychogenic megacolon." Given a physiological trigger, it still required the intervention of parent–child conflict over bowel function to evoke the state of chronic and intractable obstipation which I was describing.

The mandate for my intervention in each of these cases was the complete failure of traditional methods of treatment to resolve the symptoms on a long-term basis; despite, in the majority, heroic use of purgatives. In one child of 2½, the prescription of half a fluid ounce of cascara sagrada, t.d.s., had failed to produce a single motion over a period of seven days, and in the course of 18 months over 100 enemata had been administered without altering the clinical picture of continued obstipation with overflow soiling. It was only when this symptomatic approach was superseded by a more comprehensive therapeutic programme, including study of the basic psychogenic factors and their correction, that resolution of symptoms, on a longe-term basis, was achieved.

I entirely agree, as I said in my original paper, that psychiatric treatment, in these cases, should not be practised to the exclusion of the paediatric approach, but equally we must not discount the contribution of child psychiatry in a field previously considered the exclusive province of the paediatrician. I respectfully submit that in both groups of cases, described by Drs. Coekin and Gairdner, psychogenic factors are of aetiological importance, and should not be discounted in the mechanical group, any more than they are admitted in the second group.—I am, etc.,

Department of Child Health, University of Liverpool. PHILIP PINKERTON.

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SIR,—The article by Drs. Marian Coekin and Douglas Gairdner on "Faecal Incontinence in Children" (October 22, p. 1175) prompts me to write about a boy of 13 years brought to me by his mother. She told me he dirtied his pants usually on his way home from school. He had recently joined a new school. In view of his dislike of the new school and the strained atmosphere at home between his father and mother, the condition was diagnosed as one of psychogenic encopresis. Various drugs were tried, but without success. I then asked the mother, in the presence of the boy, who washed the dirty pants. She told me she had to wash them. I told her to make the boy wash his own dirty pants. Since then there have been no dirty pants to wash.—I am, etc.,

Liverpool, 18. H. J. PRATAP.

Demethylchlortetracycline

SIR,—It is important, I feel, to comment on one aspect of the valuable review article (October 1, p. 959) on demethylchlortetracycline (DMCT) by two of the world's most distinguished exponents of antibiotic medicine, Dr. Maxwell Finland and Professor L. P. Garrod. From what follows, it should not be construed that the conclusions the authors arrive at are challenged, but that some of the reasoning on which they are based may be erroneous. I am referring to the method of measuring the relative antibacterial activity —the use of "tetracycline equivalents."

An antibiotic assayed by the cylinder plate method is placed in cups on agar surfaces seeded with a test organism (*B. cereus* in this instance). The plates are incubated and the diameters of the zones of inhibition are measured. The diameters are converted to concentration of antibiotic by using a standard curve obtained by testing known amounts of the self-same antibiotic against the same organism under identical conditions. The curve may be constructed by plotting the logarithm of the concentration of antibiotic on the abscissa against the diameter of the zones of inhibition. In this way all the requirements of a biological assay are fulfilled—that is, the only thing differing between the unknown and the standard is the concentration of the same drug.

If it is assumed that tetracycline (TC) and DMCT have a similar action on *B. cereus*, then the standard curves for each must be parallel or else the hypothesis of similar action fails. If, as is stated, DMCT is 3.1 times as active as TC, then the standard curve for DMCT must lie to the left of that for TC by an amount equal to the logarithm of 3.1; if it does not, the statement of potency cannot be entirely correct. Had the *Str. pyogenes* been used as a test organism the curve for DMCT would have been log 2.2 to the left of TC; if the *Staph. aureus* had been used the difference would have been log 1.5, and so on. If an organism more sensitive to TC than DMCT were used the curve for the latter would have been moved to the right of the former. Now, presumably "tetracycline equivalents" are concentrations of TC that, theoretically, would have given zones of inhibition of *B. cereus* of the same diameter as those actually obtained with DMCT—that is, in assaying DMCT to obtain "tetracycline equivalents" the standard curve for TC was used instead of that for DMCT. It does not take much calculation to arrive at the conclusion that if *B. cereus* is used as the test organism, in each instance the "tetracycline equivalent" will be precisely 3.1 times the actual concentration of DMCT; if the streptococcus had been used the "tetracycline equivalent" would have been 2.2 times the actual concentration; with the staphylococcus it would have been 1.5 times the amount of DMCT. If an organism more sensitive to TC than DMCT had been used the "tetracycline equivalent" would have been less than the concentration of DMCT. Or, to put it briefly, the relationship between "tetracycline activity" and concentration of DMCT depends entirely on the organism chosen for the assay. By choosing the appropriate organism the activity of DMCT may be varied at will to be greater or less than TC or even any of the other drugs in the same group.

The activity of an antibiotic in clinical practice is modified by two factors among others—firstly, the blood level obtained, and, secondly, the sensitivity of the particular organism in question. The use of "tetracycline activity" is presumably an attempt to combine these. But, if a property of DMCT is "an activity against most bacteria exceeding that of TC by approximately twofold," it is hardly appropriate to choose *B. cereus*, about which it is stated "the factors by which the activity of DMCT exceeded that of TC against the three organisms used in these assays were *B. cereus* 3.1 . . ." It is obvious that

such a device leads to the exaggeration of the activity of DMCT as compared with TC.

The foregoing criticisms may be found not to matter very much in practice with DMCT, but let us examine the case of chlortetracycline (CTC): in Fig. 2 of Finland and Garrod's paper it seems plain that the blood levels obtained with chlortetracycline are very much less than with tetracycline—this accords with the authors' statement that "TC produced higher and better-sustained levels of antibiotic activity in the blood than OTC, and more particularly than CTC, the exceptional instability of which explains this difference." It is therefore with some surprise that one finds in Fig. 3 and Fig. 4 that CTC is apparently far superior to tetracycline in "antibiotic activity" if one uses the same criteria for its activity as was used for DMCT. Taking all these points into consideration, the conclusion that there is some inconsistency resulting from the use of "tetracycline equivalents" seems inescapable.

It is possible to conceive of a comparative test for antibiotic activity between antibiotics of similar composition. The first stage would be to obtain serum samples from people that had taken the drugs under comparison; a method which Dr. Finland has so frequently and successfully exploited to allow for the variations that occur in the body. The second stage would be to test the drugs in the samples by the cylinder plate method against not a single nor even a few assay organisms, but a randomly selected array of recently isolated organisms from patients with infections. The purpose of this would be to allow for the variations in sensitivity of the generality of organisms to the drugs under comparison. One would then measure the diameters of the zones obtained with one antibiotic, average them, and compare the result with those of other antibiotics treated in an identical way on the same array of recently isolated organisms. At least in theory this method would have the merit of taking into account the variation of sensitivity of various organisms to the different antibiotics, and, on the face of it, it would seem much more revealing than using a laboratory strain of an organism that, in any event, is not considered a pathogen.

An additional point should be borne in mind when comparing two different antibiotics by agar diffusion methods. Differences between the diameters of inhibition zones may not be due only to differences in potency of the antibiotics and in sensitivity of the bacteria being used, but may also be completely or partly due to differences in the ability of the antibiotics to diffuse through the agar. There is no reason why such differences should not occur between fairly closely related antibiotics, especially if they show clearly different properties *in vivo* as do TC and DMCT.—I am, etc.,

Department of Bacteriology, Winnipeg General Hospital, Canada.

PETER WARNER.

Complications of Immunization

SIR,—It is important to realize that immunizing procedures can occasionally cause serious brain damage, and we are glad that Dr. Justus Ström (October 22, p. 1184) has drawn attention to this fact. As he says, this is often difficult to prove in individual cases, but in one clinical syndrome we have become increasingly convinced that the brain damage is at times due to immunization (not always against pertussis). This syndrome, infantile spasms (salaam spasms, lightning fits) with mental retardation, is in approximately half the cases the result of brain damage in the perinatal period, and mental retardation in these cases dates from birth.[1] Rarely other causes such as phenylketonuria, tuberose sclerosis, or cerebral agenesis are found. In the remainder, the cryptogenic group, there is no relevant history and mental development is normal until, at about six months of age, infantile spasms appear; rapid mental regression usually follows shortly afterwards.

Following the suggestion of Baird and Borofsky[2] that diphtheria–pertussis immunization might be a causative factor, we have inquired into the history of immunizations and vaccinations in 31 patients in the cryptogenic group. Twenty-one had had one or more immunizing procedures. In 11 of these the first spasm occurred within one week of the immunization: Diphtheria–pertussis, 7 patients; smallpox, 3 patients; poliomyelitis, 1 patient (he had developed hemiparesis following an injection of diphtheria–pertussis antigen two months previously).

It is easy to dismiss such an association as coincidence, particularly since a large number of infants are being immunized at this age and this clinical entity is rare. However, in each case the history is impressive. Moreover, we cannot be sure that immunizations were not to blame in the other immunized children, even though the parents did not associate them with the onset of the illness, for in several cases the relevant dates were not precisely known. The histories of two patients whose brain damage was due to perinatal factors are also of interest. In one the spasms started two days after the first diphtheria–pertussis injection, and became more frequent after the second injection. The other showed a definite increase in the frequency of spasms immediately after his first diphtheria–pertussis injection.

For the individual family the illness is a tragedy. Although the epilepsy and accompanying E.E.G. abnormality can often be abolished by corticotrophin, mental improvement is rarely complete.[3] It seems important that in future the immunization history of these children should be carefully inquired into so that the role of these procedures in the aetiology of this syndrome can be assessed more precisely: the question of the wisdom of universal pertussis immunization, raised by Dr. Ström, may then require serious consideration.—We are, etc.,

The Children's Hospital, Birmingham, 16.

B. D. BOWER.

All Saints' Hospital, Birmingham, 18.

P. M. JEAVONS.

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SIR,—With reference to the statement by Dr. Justus Ström in his article on the complications following pertussis vaccination (October 22, p. 1184), that no neurological complications have been known to follow poliomyelitis vaccination, I would like to draw attention to the fact that at least three such cases have been published[1–3] and a fourth is at present in the press.[4] Of these four recorded cases two, both occurring in young children, were fatal, whilst the remaining two, both adults, recovered to a greater or lesser extent over the course of several months.

Whilst the incidence of serious neurological sequelae to poliomyelitis vaccination is probably extremely low (Liebe and Wöckel[5] state that their published case was

the only known complication occurring in over 5,000 vaccinations), the fact that such complications can occur is surely worthy of notice.—I am, etc.,

Copenhagen, Denmark. JILL N. GORDON.

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Salicylate Poisoning

SIR,—We think that you are to be congratulated on the opening sentence of your annotation on salicylate poisoning (October 22, p. 1216), in which you state that "the basic principles in dealing with any ingested poison are to eliminate it and to counteract the mechanisms by which it endangers life." We are surprised that you attribute so little importance to hyperpnoea as a mechanism whereby this poison endangers life, and omit to mention the simple means by which it may be counteracted.

You list the important effects of salicylate intoxication as hyperpyrexia, respiratory alkalosis, metabolic acidosis, dehydration, and ketosis. All these are the secondary effects of the hyperpnoea, and if this is abolished in the early stages of treatment they will be minimized. The hyperpnoea of salicylate poisoning will produce very low pCO_2 values (17 mm. Hg in one of our cases). Such a pCO_2 level gives rise to a marked compensatory metabolic acidosis—this is the main cause of the secondary acidosis, not, as you suggest, the presence of the salicylate radical. Having, as it does, an equivalent weight of 137, it is unlikely in clinical conditions to contribute more than 3 mEq/litre to the total fixed acid of the extracellular fluid. The hyperpnoea will also, in children, by virtue of the tremendous muscular work involved, increase the metabolic activity and therefore the body temperature. If this work is abolished the temperature falls rapidly, in one of our cases from 102.4° F. to 98.4° F. (39.1–36.9° C.) in two hours without the use of other aids for reducing temperature. Due to the hyperpnoea the muscle activity capable of producing such an elevation in temperature would obviously also produce some degree of ketosis, and the concomitant sweating will result in gross dehydration.

We were surprised that your annotation did not mention the method discussed independently in the British[1] and Scandinavian[2] literature of treating salicylate poisoning by curarization and controlled ventilation. If this is done all the major manifestations of the salicylate intoxication that are secondary to the hyperpnoea will be abolished, and thus when the blood concentration has been reduced to a non-toxic level by the kidneys, usually in 10 to 18 hours, the patient will recover uneventfully. This method, if employed under the supervision of a skilled anaesthetist, would seem to offer the great advantage of "counteracting the mechanisms by which life is endangered." This is a simple, safe, and rational procedure infinitely preferable to the use of acetazolamide, which could only accentuate the metabolic acidosis, or to the use of the artificial kidney, which carries an appreciable mortality and may be impracticable for infants.—We are, etc.,

G. JACKSON REES.
ALAN L. STEAD.
G. H. BUSH.

Department of Anaesthesia,
Alder Hey Children's Hospital,
Liverpool 12.

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Salicylate Dementia

SIR,—A 62-year-old Yugoslav woman, who spoke no English, was sent to the local hospital because she appeared to be going mad. Her behaviour during the first few hours after admission rather confirmed this view: she was very restless, shouting and moaning and wringing her hands. On examination I noticed that she had a rapid pulse and was sweating, even after sedation; she was certainly not thyrotoxic. Three days later it was possible to get a full history through an interpreter. The patient's only complaints were that she felt she was going out of her mind, and that from time to time she had pains in her belly. Eighteen months previously she had had a thumbnail removed, in another town, for chronic paronychia, and a doctor had told her to take two aspirin tablets every four hours after the operation. When in due course her paronychia recurred, the patient had gone back to her tablets, and had taken 40 gr. (2.65 g.) of aspirin every day for the next seventeen months. Stopping the tablets led to full recovery.

This case seemed worth reporting because none of the textbooks of pharmacology or psychiatry of medicine that I have been able to see mention the possibility of chronic salicylate poisoning *presenting* as dementia, without any of the other florid signs of salicylism.

Tailpiece: The patient's neighbour, when told the diagnosis, exclaimed: "I've been telling her to stop those tablets for the past year. I knew they were poisoning her."—I am, etc.,

Waroona,
West Australia. PAUL MESTITZ.

Hypotensive Effect of Perphenazine

SIR,—A patient was recently admitted to the Queen Elizabeth Hospital after attempting suicide with a combination of "tuinal" and "fentazin" (perphenazine). Her subsequent progress is recorded.

Mrs. X, a known chronic schizophrenic aged 40, was admitted in coma on April 25, 1960, at 3.30 p.m., having taken an overdose of tablets—40 4-mg. fentazin tablets and 6–12 3-gr. (0.2-g.) tuinal tablets (a mixture of quinalbarbitone gr. 1½ (0.1 g.) and amylobarbitone gr. 1½ (0.1 g.)) probably some six hours prior to admission. On examination she was deeply comatose and unresponsive to painful stimuli. The pupils were fixed and dilated and the deep reflexes diminished. Her plantar responses were flexor. Pulse and blood-pressure were satisfactory, as were her respirations, though for a time the latter were very shallow.

Initial therapy consisted in gastric lavage and intravenous injection of 30 mg. amiphenazole and 200 mg. bemegride. She was also given prophylactic penicillin. Following this, her reflexes became quite brisk and pharyngeal and laryngeal reflexes returned. To prevent deepening of her coma, and, if possible, to counteract the hypotension which was anticipated as a possible side-effect of perphenazine overdosage, she was also started on methylamphetamine hydrochloride, 30 mg. intramuscularly every four hours. However, nine hours after admission the blood-pressure fell to 60/0 mm. Hg, and to restore it a noradrenaline drip containing 8 μg. per litre was erected. 24 hours later, as it appeared likely that supportive treatment would be required for some time, the noradrenaline was replaced by metaraminol initially 200 mg. per litre eight-hourly and later 400 mg. per litre 12-hourly. It was necessary to continue this until May 1 in order to maintain systolic blood-pressure of over 100 mm. of mercury. No effect was obtained when the drip was stopped and the pressor agent administered intramuscularly.

Prolonged hypotension of this sort in a patient who had regained her reflexes within two to three hours of admission and who was fully conscious within 48 hours is unlike anything we have encountered in barbiturate overdosage: we therefore think that it may be a side-effect of the perphenazine perhaps potentiated by barbiturate taken at the same time. In reviewing the literature, cases of perphenazine overdosage or idiosyncrasy are rare, though hypotension has been reported in some normal subjects following intramuscular injection. It was also reported in a 15-year-old schizophrenic boy who was taking up to 24 mg. a day; though in this case recovery both from the hypotension and a severe Parkinsonian state (also assumed to be a side-effect of therapy) occurred in 24 hours.—We are, etc.,

G. D. MIDDLETON.
F. CLARK.

Bensham General Hospital,
Gateshead, Co. Durham.

Concept of Collagen Diseases

SIR,—I do not entirely disagree with Dr. A. H. T. Robb-Smith's desire to retain the concept of collagen disease (October 29, p. 1308), but to be useful this concept might seem to need some clarification. It is obvious that the various functions of the body require the presence of elaborately specialized structures composed of substances which, although produced by cells, are in the main anatomically extracellular. Such are the lens of the eye, the vitreous humour, bone, fibro-cartilage and cartilage, and such condensed systems of collagen fibres as tendons, ligaments, the dermis, and the heart valves. The critical questions would seem to be whether changes in these extracellular substances can occur independent of cellular or vascular derangement in their neighbourhood, and if so whether these apparently spontaneous extracellular changes may be regarded as the salient feature in a clinically distinct group of diseases. These questions have not, I think, been decided yet, but it is probable that their solution must require methods other than those of classical histology, since these, elegant as they are, have been developed mainly for the study of the cells rather than of the non-cellular components of the tissues. It would perhaps be advantageous also if the changes observed in extracellular structures came to be called by names other than those used in cellular pathology. The term necrosis, for example, as applied to collagen fibres is meaningless, since a thing cannot die which has never, properly speaking, lived.—I am, etc.,

T. D. DAY.

Department of Experimental Pathology
and Cancer Research,
School of Medicine, Leeds 2.

Pre-operative Disinfection of the Skin

SIR,—The excellent article on disinfection of the skin of operation sites by Dr. E. J. L. Lowbury and his team (October 8, p. 1039) will have interested most surgeons who still look for the ideal skin preparation. I found it incomplete, however, as only the aqueous solution of "penotrane" was used, whereas even the makers of penotrane suggest that the 0.1% solution in alcohol is their most effective pre-operative skin preparation. The comparison of penotrane in water with other skin disinfectants, therefore, does not give the whole picture. For two years I have regularly used 0.1% solution of penotrane in alcohol without trouble and with the added advantages that it is effective in the presence of blood and its deeper penetration of the skin is probably beneficial in a long operation when deeper-seated organisms in sweat glands and hair follicles approach the surface.—I am, etc.,

G. S. LESTER.

Marston Green Maternity Hospital
and Hospital for Women,
Near Birmingham.

Child Psychiatry

SIR,—The team approach in child psychiatry, as practised in this country, is the envy of other nations. I can see from Dr. Louise F. W. Eickhoff's letter (October 22, p. 1234) what type of experience she may have had with it and, obviously, some of it has not been too pleasant.

I have always found that the difficulties, such as "wastage of psychiatric time in the idealistic approach," could be overcome in a team where the psychiatrist is *primus inter pares*. The investigations of the educational psychologist are quite irreplaceable in the full assessment of a child and are not to be replaced by inspired guesswork and intuition. The report of the psychiatric social worker will always save a great deal of psychiatric time, even if the psychiatrist insists on going over the whole field again with the patient. There is absolutely no necessity for time-consuming case conferences if friendly interchange and day-to-day contact are cultivated in the clinics between the team members. There should be no necessity for an automatic throwing into action of the whole team if the psychiatrist indicates in each case what he requires from the other members of the team. Similarly as he will, for instance, give opinions on children that were directly referred by the school to the School Psychological Service, as their consultant. There is no doubt that difficulties will arise in teams, but as in psychiatry, particularly child psychiatry, we are all expected to be experts in personal relations, these difficulties should be overcome.

Whilst the consultant children's psychiatrist should have a wider field than the local child guidance clinic offers, and seek his work in hospitals, institutions, etc., and while he needs to fall back in many instances on the general medical services as consultant and also ancillary aids to his own work, it would have to be deplored if in-roads were made on the traditional, well-established, and irreplaceable child guidance clinic services and its team. In other words, there is room for much expansion and none for contraction. If it is a matter of psychiatric time only, I may say that there is, in practice, no waiting-list in my clinics and there is no good reason for an alleged lack of children's psychiatrists, except the unwillingness of authorities to create posts. These will, if present, be filled in the course of time as the delicate but sensitive balance of supply and demand dictates. If it is argued that this is not borne out by the present supply, one can only say look into the advertising columns of the *B.M.J.* and you will agree that there is no great public and advertised demand for the services of children's psychiatrists.—I am, etc.,

D. J. SALFIELD.

Child Guidance Service,
Derbyshire County Council.

School Phobia

SIR,—I should like to thank Dr. R. T. D. Franklin for his letter (October 22, p. 1238) explaining the genesis of school phobia. He explains that it is a symptom of an anxiety neurosis due to bad upbringing. Modern parents have replaced summary punishment by disapproval. The prolongation of disapproval produces a vicious circle in which parental hostility generates child anxiety, and this in turn leads to further irritation.

All this is true, and was stated in bolder terms 3,000 years ago by the writer of proverbs in the Old Testament, "He who spares the rod *hates* his son, but be who loves him is diligent to discipline him" (Proverbs xiii. 24). In throwing over the fundamentalism of our forefathers, we have lost the only foundation on which a healthy society can be built—namely, sound parental discipline reinforced if necessary by summary punishment—"Do not withhold discipline from a child; if you beat him with a rod, he will not die" (Proverbs xxiii. 13). Disbelief in this teaching is the root cause of many of our social ills. It is largely responsible for the delinquency, irresponsibility, and the general frustration of youths who have no standards to look up to and respect. Instead, we have adopted a false philosophy of the inherent goodness of man. This has led to the false psychology of the importance of the natural ego which must not be frustrated. This, in turn, has led to all the false systems of parenthood and child-care which are based on the theory that nothing is to be gained by punishment.

Although experience teaches that the Bible view of parental discipline is right, it is considered old-fashioned and barbarous to suggest this. It is strange that in a so-called Christian country we deny a principle which lies at the very heart of Christian philosophy. This is expressed most forcibly by the writer of the letter to the Hebrews: "For the Lord disciplines him whom He loves, and chastises every son whom He receives. If you are left without discipline, in which all have participated, then you are illegitimate children and not sons. For the moment, all discipline seems painful rather than pleasant; later it yields the peaceful fruit of righteousness to those who have been trained by it" (Hebrews xii. 6, 8, 11).

Doctors could do a great deal more to help modern parents with behaviour problems if they themselves had a sound philosophy of parenthood. The above quotations wisely applied early in childhood would prevent a vast amount of misery both among parents and among children.—I am, etc.,

Bridgend General Hospital, Bridgend, Glamorgan. A. W. FOWLER.

SIR,—Your leading article (September 17, p. 848) equates school phobia with school refusal. Neither it nor subsequent correspondents mention the factor of simple prolongation resulting from the stand that the child has taken and the loss of self-esteem that he faces in coming off it, even after extensive psychiatric and social work has, to say the least, assuaged the salient factors. At this point a stand firmly made not only obviates the insecurity of prolonged, non-punitive disapproval which my friend, Dr. R. T. D. Franklin (October 22, p. 1238), rightly stresses, but also both provides the child with important training in the acceptance of civic duties and supports the parents and school-attendance officer in their normal authority.

It is of no value to a child to be able indefinitely to flaunt the law, particularly in these present standardless times. Some time ago, two children, permitted till then to stay months off school, came under my care. After full explanation of all overt dynamic factors, both were clearly instructed upon their legal duties of school attendance and the legal sanctions that continuation of refusal to attend would entail. Both returned promptly to school, were followed-up, and were seen to gain overtly, not lose, from coming off their high-horses, the defeat of their stand being offset by their victory over the disability. Both were amenable to retrospective analytical understanding of the revoke.

It is as easy in the management of these as of neurosis in general to let psychodynamic theory run away with wisdom.—I am, etc.,

Wonford House Hospital, Exeter. SEYMOUR SPENCER.

"Winkle-picker's" Disease

SIR,—In respect of Dr. David F. Thomas's letter (October 15, p. 1164), may I refer him to *Cunningham's Text-book of Anatomy*," eighth edition, page 515, where the following sentence occurs: "Its [extensor hallucis longus] tendon passes over the dorsum of the foot to be inserted into the base of the distal phalanx of the big toe."—I am, etc.,

Liverpool 20. M. MACLEOD.

"Troubadour Shoes"

SIR,—Following Mr. J. N. Wilson's acute description of "Winkle-picker's Disease" (September 24, p. 944) we have had a discussion on television by an orthopaedic surgeon and members of the public on foot deformities and disabilities due to the prevailing fashion in shoes. It is worth noting, however, that foot deformities with pain or discomfort may occur even though there is plenty of room in the shoe or boot for the foot. Just as important as the shape of the shoe is the way the foot is held in the shoe. Some of the worst foot deformities I have seen were in men wearing large boots with plenty of room to hold the foot correctly, if only they would. On the other hand, I know sensible women who have been made to realize how to hold the foot correctly and who would not hesitate on occasion to wear the "Winkle-picker" shoes Mr. Wilson rightly condemns. The foot will stand a lot of misuse and yet remain improvable if not entirely corrigible.

Besides the "Winkle-picker," if my observation is correct, there has appeared recently a type of shoe pointed in the toe but very much longer than the foot. It is the sort of shoe, if my memory of childhood's stories serves me truly, worn in the Middle Ages. Blondel, the detective-minstrel, "*spähend nach dem Eisengitter vor dem Schlosse Dürrenstein*," wore such a shoe, so that it might be called the Blondel or the Troubadour shoe. Such a shoe with a heel giving stability would be entirely harmless. It would give room for the toes to be held straight in line with the metatarsals and slightly flexed to be part of the whole plantar arch of the foot. In moments of physical or emotional stress a woman tends to cock up her toes; in more decorous words, to extend the metatarsophalangeal joints and then put her weight on the capsules of these joints stretched between the separated bones. When showing a doctor her feet a woman will so present them with the extensor tendons as cords showing high above the level of the surrounding skin. It does not occur to her that there is anything abnormal in so holding a resting foot. No wonder that she gets callosities over these joints below, and a row of corns where the toes rub against the roof of her shoe, and no wonder she gets a feeling of comfort and relief when the metatarsal arch is raised and she is persuaded to hold her toes as part of the

whole arch of the foot, so that the calloused places can be massaged backwards and cease to be callous and the corns on the toes can be peeled off. Suitable exercises and recollectedness, while at work or standing at rest, how the feet should be held will complete the cure.—I am, etc.,

Reading, Berks. E. H. STRANGE.

Sewage in the Sea

SIR,—There continues to be correspondence on the above subject. It is, of course, consequent upon the debate at the Annual Representative Meeting, Torquay (*Supplement*, June 25, p. 394). At that meeting the *Daily Mail* asked for a doctor qualified in public health to assist them in an investigation of this matter, and I was recommended. I visited between 25 and 30 seaside resorts, all of which disposed of their sewage in the sea. The conclusions I arrived at were:

(1) That every seaside town was desirous of taking such steps as might be considered desirable for improving their disposal methods if necessary.

(2) No medical officer of health to whom I spoke had any knowledge of persons contracting any illness through bathing at his town's beaches.

(3) This fact was stressed to me on numerous occasions as militating against any recommendation he might make to his council for improving sewage-disposal methods. He was met with, "What proof have you got, Doctor, that there is any danger to health from our present methods?" He could only reply, "None" and speak of possible potential risk, which carried no weight at all.

(4) In effect, the findings of the Public Health Laboratory Service were confirmed completely.

(5) A case was quoted to me of a child of 6 who developed poliomyelitis ten days after a bathe in a sea where her father had observed sewage outfall. But in the above report it was stated that the virus of polio had not been found in sea-water. If it had been found, for how long would it live in that hyperchlorinated solution? Also, how had it got there—from a patient or carrier of polio on shore? Could not the child have caught her infection by contact with such persons?

(6) Sewage disposal at sea should be at ebb tide with the outfall pipe a mile or more out to sea, and an outgoing current should prevail. Before discharge sewage should be well screened and solids removed. Their use as a source of methane was exploited at a good financial gain in one town. Such was the disposal at many places. A very large town has a £3m. scheme to remove all sewage disposal from sea to land. That is an example of the very heavy cost which might fall on a seaside town, and even improvement schemes were stated to be extremely costly. No Government grant is forthcoming: is it because no health hazard has been *proved*?

(7) My investigations covered two weeks and I contacted medical officers of health, also the borough engineer, and sometimes the town clerk. I visited all the beaches, saw the sewage outfalls, and especially inquired as to complaints which might have been received. Complaints had been few or absent. I saw no sign of sewage pollution.

(8) So far as the places I visited go I would thoroughly endorse the findings of the Public Health Laboratory Service inquiry that no danger to health had been proved and no "scandal of the beaches" was apparent to me in those beaches I visited.—I am, etc.,

Guildford, Surrey. F. A. BELAM.

Fringe Medicine

SIR,—The average sick person is usually looking for a little sympathy and understanding in the treatment of his illness, and it is for this reason that the practitioners of "fringe medicine" (October 29, p. 1299) prosper. If they were to adopt the indifferent and increasingly brusque manner of so many of the National Health doctors, they would be unable to earn a living. It is for the same reason that those of us who practise private medicine outside the Health Service are still able to make a somewhat meagre living, in spite of the fact that the patient has to pay for his expensive medicines and appliances, which he has already paid for very heavily in taxation and contributions. The unqualified practitioner has an advantage over the qualified practitioner from this point of view, as, for the most part, he does not prescribe either drugs or appliances. The Government—Socialist and Conservative alike—have been determined to stamp out private practice altogether by their persistent refusal to allow the private patient drugs and appliances, which are his due, and by their determination to lavish free treatment, free medicines, and free hospital accommodation on any sickly foreigner who may visit our shores, in spite of the fact that there is no reciprocal arrangement.

The medical profession opposed a National Health Service because they feared that they might become bureaucrats and civil servants, and their fears have been more than justified.—I am, etc.,

Camberley. LESLIE HARTLEY.

Crèche for Nurses' Children

SIR,—With the prevailing shortage of nurses many hospitals employ married nurses part-time, and find them a great help in staffing the wards. Such nurses can more easily return to hospital work if their children are satisfactorily cared for during the day. We have been exploring the possibility of starting a crèche cum nursery-school at this hospital for the children of married trained nurses. There are clearly a number of difficulties in implementing such a scheme. I would be most grateful if anyone with experience of anything like it would write to me and tell us their experience.—I am, etc.,

N. F. COGHILL,
Chairman, Hospital Medical Committee,
Isleworth, Middlesex. West Middlesex Hospital.

POINTS FROM LETTERS

Ferrous Fumarate and Occult Blood Tests

Drs. T. D. S. HOLLIDAY and I. M. CUTHILL (Chester Royal Infirmary) write: We must apologize for an error in our letter (October 29, p. 1310). Positive occult blood tests were produced in the healthy antenatal patients within three days, and not three weeks as previously stated.

Prevention of Migraine

Dr. M. ASTON KEY (Southsea) writes: In the interesting article by Dr. Rodney Grahame on the response to drugs of migraine patients (October 22, p. 1203) we were not told much of the ophthalmic conditions of the patients. The late Dr. A. P. Beddard, physician of Guy's Hospital, was a fellow student of mine in the early 'nineties. He began to get some migraine attacks, occasionally falling down unconscious in the Underground Railway and having to be lifted out at the next station and laid on the platform till he regained consciousness. He consulted five London oculists without benefit, and, when he consulted the sixth, his glasses cured him straight away: a very accurate correction of slightly mixed astigmatism. . . . Would it not be interesting to learn more fully of the ophthalmic conditions of these patients?

Obituary

J. E. PATERSON, M.B., Ch.B., F.R.F.P.S.

Mr. J. E. Paterson, formerly senior neurological surgeon to the Western Regional Hospital Board in Scotland, died suddenly at his home in Rothesay, Bute, on October 26. He was 70 years of age and had been living in retirement since 1955.

James Eric Paterson was the son of a Glasgow medical practitioner, and graduated M.B., Ch.B., with honours, at the University of Glasgow in 1911, being awarded the Brunton memorial prize as the most distinguished graduate of his year. After graduation he entered into practice with his father till the onset of the first world war, when he joined the R.A.M.C. and went on active service, being decorated by the French Government for his work during an epidemic of typhus. Returning to Glasgow, he re-entered general practice, but obtained a surgical appointment at the Royal Infirmary shortly afterwards and combined this with his work in practice.

In the latter part of the 1920s he was offered, and accepted, the post of surgeon to Stobhill Hospital, Glasgow, then under the corporation, and devoted his whole time to surgery. He became interested in the developing specialty of neurosurgery, and in 1930 spent a year at the Mayo Clinic and with Harvey Cushing. Returning to Glasgow, he began with a small team to develop neurosurgery along modern lines, and in a short time gained a very considerable reputation. Although combining his specialty with general surgery, he was invited to join the staff of the Victoria Infirmary, Glasgow, in 1933, as neurosurgeon, and shortly afterwards obtained a similar appointment to the Royal Hospital for Sick Children, Glasgow. In 1940 he was appointed to take charge of the newly opened neurosurgical unit at Killearn Hospital under the auspices of the Emergency Medical Service. He still, however, retained his interest in general surgery at Stobhill Hospital until the beginning of the National Health Service, thereafter confining himself entirely to neurosurgery till his retirement. At the Annual Meeting of the B.M.A. in Glasgow in 1954 he was a vice-president of the Section of Neurology.

James Eric Paterson was of a medical generation in Glasgow which produced men of very great quality, and among these, in memory, he will take his rightful place. He himself would not have regarded his work in surgery and his achievement as anything extraordinary, but it was. His chosen path was never one which could be easy. There were never any great financial rewards to be gained, but there was a great deal of pioneering work to do. It was typical of his energetic personality that he built the foundations of a general surgical unit in Stobhill Hospital at the same time as he was developing his pioneering work in neurosurgery in the region. Paterson was widely known for his neurosurgical work, but it is not so widely recognized that he was a first-class general surgeon with an impeccable technique and always conversant with the recent advances. Those who worked with him in general surgery and in his early days as a neurosurgeon formed an admiration for him, both as a surgeon and as a man, which grew with the years, and developed an affection for him which remains undiminished.

A man of very wide culture, he was an active member of the Royal Philosophical Society of Glasgow and latterly its librarian. There were few subjects on which he had not at least some knowledge, and he was an amateur geologist and botanist of ability. In his middle years he became an enthusiastic yachtsman, and it was his great joy to cruise in the company of one or two friends among the Western Isles. He learned more about sailing and navigation in a few years than many men would do in a lifetime. Not content with an academic interest in art, he began to paint some years before his retirement. This he did very well; and in his retirement he combined his botanical and geological expeditions with water-colour sketching.

James Eric Paterson was a man of small stature but of great heart and mind, and it was a great privilege to work with him and to be admitted to his friendship. The sympathy of all his colleagues in the West of Scotland goes to his widow and his two sons.—J. F. G.

J. S. R. writes: The development of neurosurgery in the West of Scotland owes a great debt to Mr. J. E. Paterson: first as a pioneer, and then by his co-operative spirit and enthusiasm he made a united unit possible. Although a man of definite opinions he was always tolerant, receptive of new ideas, and ever ready to help and advise: he was never dogmatic. He was an ideal senior colleague. His chief neurosurgical interest was in tumours of the pituitary and other lesions in the region of the optic chiasm. Though his publications were few he gave many excellent papers on this and other subjects. Outside medicine his interests were wide and his circle of friends correspondingly large, but his chief hobby was yachting, and it was characteristic of him that he did not race or attempt the spectacular but found pleasure in cruising in the territory of the real expert —the Western Isles. In his retirement he chose to live in Rothesay in full view of the Clyde estuary, which he loved. Though he was no longer able to sail, his other interests were so numerous, in particular painting and botany, that he led a very full life in his retirement.

H. H. BLAKE, O.B.E., M.B., B.S.

Major-General H. H. Blake, who was assistant director of medical services at Aldershot during the second world war, died at his home at Brockenhurst, Hampshire, on October 14. He was 77 years of age.

Harold Henry Blake was born at Yarmouth on August 1, 1883, and was educated at Framlingham College, Suffolk, the University of Durham, and St. George's Hospital, London. After graduating M.B., B.S. in 1907, he held the post of house-surgeon at the Royal Cancer Hospital in London and then entered the R.A.M.C. in 1908. He was in India until the outbreak of the first world war, during which he served in France and Belgium, being twice mentioned in dispatches. He was appointed O.B.E. in 1919, and returned to India in 1921, serving there until 1932 and taking part in operations on the North-west Frontier in 1930–1. Promoted colonel in 1935, he was for some years thereafter in Hong Kong, where he was president of the Hong Kong and China Branch of the British Medical Association from 1936 to 1938. On the outbreak of the second world war in 1939 he was given the acting rank of major-general and appointed deputy director of medical services in the Western Command. Due to retire from the Army Medical Services in 1940, he was re-employed for a further three years, being assistant director of medical services at Aldershot from 1941 to 1943. When he left the Army he was granted the honorary rank of major-general and appointed superintendent of the Stoke Mandeville Hospital until the end of the war. During the last few years of his life he lived at Brockenhurst. He leaves a widow and one son and a stepdaughter and stepson.

G. M. THOMSON, M.D., M.R.C.P.Ed., D.P.H.

Dr. G. M. Thomson, who was senior specialist in social hygiene in the Hong Kong Government Medical and Health Service, died in Oslo on October 8, after a brief illness. He was 47 years of age.

Born in Edinburgh on December 15, 1912, Graham Murray Thomson was educated at Daniel Stewart's College and at the University of Edinburgh, where he graduated M.B., Ch.B. in 1935. After holding appointments in Edinburgh and Chester he took the D.P.H. in 1938. In October, 1939, he joined the V.D. section of the Edinburgh Corporation's public health services and was appointed a

clinical assistant to the Edinburgh Royal Infirmary in 1941. He held this post until 1944, when he joined the R.A.M.C. as a specialist venereologist. He proceeded to the M.D. in 1940 and became a Member of the Royal College of Physicians of Edinburgh in 1942.

Dr. Thomson joined the Colonial Medical Service in 1947 and was appointed adviser in V.D. control in Trinidad, in the West Indies. Five years later he was transferred to Hong Kong as senior social hygiene officer. His post was regraded to specialist rank in 1955 and he was promoted senior specialist in 1959. He became a member of the W.H.O. Expert Advisory Committee in Venereal Infections and the Treponematoses in 1958 and had been appointed a member of the Medical Council of Hong Kong shortly before his death. While in Britain this summer he attended the Annual Meeting of the B.M.A. in Torquay as a representative from Hong Kong.

In his efficient and unostentatious way Graham Thomson built up in Hong Kong a system of out-patient venereal-disease and leprosy clinics that are a model of their kind. At the same time he organized and developed a dermatology service which he rightly regarded as complementary and the key to the early diagnosis of latent syphilis and leprosy. The permanent and substantial contributions he has made are reflected by the excellent results that have been achieved during his eight years of service to the people of Hong Kong.

He always laid great stress on physical fitness and when in Edinburgh was a constant attender at Charlie Cotter's gymnasium, so well known to many Edinburgh medical students and graduates. It was during this period that, impressed by the benefits of "inducto"-pyrexia in the treatment of neurosyphilis, he himself underwent a course to gain first-hand knowledge of the effects in a physically fit individual. This is only one example of his thorough approach to clinical problems.

His untimely and tragic death has left all who knew him with a sense of irreparable loss. He was a wise and gifted clinician of great administrative ability who never spared himself. He has left a memory that will not fade easily, and he will be long and affectionately remembered by his patients and colleagues. To his widow and five children we extend our deepest sympathy.

Dr. RALPH C. L. BATCHELOR writes: Graham Thomson's service with the V.D. department in Edinburgh was characterized by outstanding zeal and aptitude for this work. He was keen to break new ground and quickly evinced a great interest in hyperpyrexial therapy as applied by the "inductotherm" fever cabinet. This new development was his pet province. Before penicillin came into general use he and other members of the staff explored the application of heat plus chemotherapy in the treatment of resistant gonorrhoea as well as in complications of syphilis like G.P.I. and tabes dorsalis. Thomson expanded his experience into a thesis which he presented for the degree of M.D. and also wrote and collaborated in two papers published in the *Edinburgh Medical Journal* in 1941 and 1942. He used the fever cabinet very freely, shepherded his charges through their ordeal, and never lost a single patient though the accepted mortality in G.P.I. was 2 to 10%.

Graham was that refreshing rarity a real enthusiast. From the beginning he put his heart and soul into venereology. Later he became adviser on V.D. control to the West Indies Governments and the huge volume of work which he undertook and accomplished, will remain a monument to his memory. Through his sudden and premature death venereology has lost a devoted worker and his colleagues a stimulating and encouraging influence for good.

J. S. MACBETH, M.B., Ch.B., D.P.H.

Dr. J. S. Macbeth, who was formerly in practice at Kibworth Beauchamp, Leicestershire, died on October 14, aged 69.

R. J. S. McD. writes: The sudden death of J. S. Macbeth in an Edinburgh nursing-home, where he was to have undergone an operation, removes a figure very familiar to all who were students in Edinburgh just before and after the first world war. He was the son of Alexander Macbeth, J.P., a solicitor in Pitlochry, and went to George Watson's College, where he gained his rugby cap for the school. At the university he took an honours degree in classics, but in 1913 he decided, like so many of his family, that medicine was his *métier*. When war broke out in 1914 he at once joined the Scottish Horse of his native county, and saw service in Macedonia. By 1918, however, the shortage of doctors allowed him to return to complete his medical degree, and during a very successful student career he got a surprising number of class distinctions for one so otherwise active.

"Jock" was at the centre of university social life in the Union and S.R.C., but particularly identified himself with the resuscitation of the Boat Club. Several successful seasons followed, during which the Edinburgh boat won the Ladies' Plate at Berwick and the Grand Challenge Cup at Durham Regatta. He was a member of the first Edinburgh boat ever to row at Henley, but the illness of another member marred the visit. He was the last surviving member of the crew.

He took a little time to settle down, but after several house posts, including one under Sir Robert Philip, and two voyages to Japan, he took the D.P.H. in 1921 and set up practice in Kibworth Beauchamp, where he was immensely popular, for his conscientiousness in everything he did was well known. He married in 1958 and retired to Berwick-on-Tweed. His widow and two stepchildren survive him.

ELIZABETH J. MOFFETT, M.D., B.Sc.

The obituary of Dr. Elizabeth J. Moffett was published in the *Journal* of October 22 (p. 1244).

F. B. writes: Dr. Moffett's parents were Irish and her father was a Congregational minister who held the then advanced view that daughters should have the same educational opportunities as sons. So Elizabeth was sent to a boarding-school for the daughters of Congregational ministers, of which the headmistress, Miss Hadlam, ranked with Miss Buss and Miss Beale. This was the first school to provide science teaching for girls. When she graduated in medicine opportunities for women doctors were few and prejudice was high. After several struggling years in general practice she entered the school medical service, first in Stafford and later in Birmingham. She was an active member of the suffragette movement, and at one point her refusal to pay taxes brought the bailiff to her home.

Throughout her long life Dr. Moffett was acutely interested in social problems, especially those concerning the well-being of children, and her zeal for righting wrongs never faltered. She had the gift of speech and with her Irish wit enlivened many a meeting and clinched many an argument with her forthright common sense. She held the esteem and affection of a host of friends in many walks of life and they will miss her greatly. To her large "family" of nephews and nieces, who with their children were a constant source of interest and pleasure, we extend our sympathy.

Medico-Legal

MENTAL HOSPITAL INQUIRY

[FROM OUR LEGAL CORRESPONDENT]

A three-man committee, under the chairmanship of Mr. F. E. Sowden, which has been inquiring into allegations about events at St. Lawrence's Mental Hospital, Caterham, Surrey, has found the allegations not borne out by the evidence (*The Times*, November 3). The inquiry was initiated by the South-west Metropolitan Regional Hospital Board as a result of complaints about the treatment of a

12-year-old-boy, Alan Smith, the son of Mr. John Smith, of Hainault, Essex. In October, 1954, Alan had been declared ineducable. On June 28, 1956, he was sent to St. Lawrence's as a certified patient, graded as an imbecile. At that time he was restless and noisy and had no powers of concentration. At first he was put in a children's ward, but in July, 1959, because of his behaviour, he was put into a male ward. In January, 1960, he was transferred to another male ward, E 1, where he remained until September 5.

Four Allegations

Mr. J. Tapsfield, legal adviser to the Regional Board, said there were four allegations which the committee had to consider: (1) That the boy should not have been kept in male ward E 1. (2) That Mr. Smith saw his son being pulled across the hospital sports field by a man. (3) As reported in the *Daily Herald*, that a male nurse had stated that the boy had twice been assaulted by a male patient aged about 40. (4) As reported in the same paper, that Mr. Smith had not objected to the authorities because he was frightened that reprisals would be taken against his son if a male nurse was disciplined.

Evidence was given by Mr. and Mrs. Smith that, on visits to Alan during his stay in the male wards, they saw that he was bruised in different places. Mr. Smith also gave evidence in support of the other allegations. Matters came to a head when, on September 4, Mr. Smith (an employee of the *Daily Herald*) took a *Daily Herald* reporter with him to Ward E 1 to visit Alan. Subsequently the reporter put certain allegations to the hospital superintendent, Dr. John Gibson. On September 6 a doctor examined the boy to see if there were physical signs of assault, and the next day the *Daily Herald* published a report headlined, "The Scandal of Ward E 1."

Other witnesses gave evidence in corroboration of Mr. Smith's allegation of acts of indecency among the patients, and the *Daily Herald* reporter, Mr. Don Cassell, also gave evidence. A student nurse admitted in evidence that he worked on the wards when inexperienced; he said he did not know the method for reporting incidents. Although he did not withdraw his allegation of indecent acts, he admitted that he made part of his statement to the reporter in a hotel or public house, having had more drinks than he was used to, so that he could not remember what he said on that occasion.

Dr. Gibson gave evidence refuting the allegations, and justifying the transfer of Alan to an adult male ward, and thence to Ward E 1. Alan was dangerous to other children in the children's ward, and so was put in a ward for males between the ages of 7 and 27. After 14 days he was put in another ward with patients between the ages of 17 and 55. There were two wards in which Alan could have been placed. One was unsuitable because of the presence of another vicious boy there; the alternative was E 1, where the patients were of the same mental age as Alan, though older in years, and it was felt that they might have a calming effect on him. In fact, in E 1 Alan's condition improved, and he received no more injuries from falls. Evidence in support was called from the hospital staff.

Findings and Recommendations

The committee announced on November 2 that they found none of the allegations proved and found that the transfer to Ward E 1 was justified. They also announced that in their report to the Regional Hospital Board they would make three recommendations: (1) That greater care should be taken by senior nursing staff in the initial instruction to student nurses before they took up duty in the wards. (2) That the Regional Hospital Board should instruct its legal adviser to investigate fully the action of the *Daily Herald* in the matters brought before the committee and that particular reference be made to the conduct of *Daily Herald* employees within the hospital and their methods of approaching hospital staff. (3) That the Regional Board should consider whether the relevant papers should be laid before the Press Council.

Medical Notes in Parliament

CARDIFF HOSPITAL CRITICIZED

[FROM OUR PARLIAMENTARY CORRESPONDENT]

Many of the criticisms that have been made by architectural, medical, and lay authorities of the design for the new University Hospital of Wales at Cardiff were brought together by Mr. LEO ABSE, Labour member for Pontypool and a solicitor, in a heavy attack against the project on November 2. His charge, in brief, was that Wales was being saddled with a museum piece: unimaginative, inflexible, almost incapable of expansion, housing a series of wretched blunders conflicting with current ideas on hospital design in a dull, cliff-like bulk of buildings, institutional in appearance. His appeal was that the Ministry of Health should call in the director of its architectural department and his research staff to make a ruthless and radical overhaul of the detailed plans, and in this way save Wales from the possibility of its most expensive administrative blunder in the post-war years.

Miss EDITH PITT, Parliamentary Secretary to the Ministry of Health, told him firmly that the promoters of the scheme —the Board of Governors of the United Cardiff Hospitals and the Welsh National School of Medicine — had wanted a hospital integrated with a medical school. The closest possible working arrangements between the professional and clinical staff, with the various departments, and their research and other laboratories all adjoining their wards and patients, was considered essential. That was what the promoters wanted. That was what they had got. Looking forward, she said that much of the criticism had been based on premature conclusions; in the process of development of sketch plans much rearrangement and replanning was being carried out.

"Ossified Design"

Mr. ABSE began his critical catalogue with the architect and assessors. Wales had asked for a teaching hospital so imaginatively and elastically designed that it would meet not only present needs but be adaptable to future and rapid changes in scientific medicine. "But this ossified hospital design, accepted from a septuagenarian architect by assessors led by another septuagenarian architect, is a design for 1950, not as it should be for a 1980 hospital. Wales wants a forward-looking teaching hospital; it is being proffered a mausoleum." The contemptuous attitude to research was well illustrated by the location and space allocated to the animal house. It was notorious in Wales that the younger members of the medical teaching staff at Cardiff were in despair that this space was minimal. Was a teaching hospital in Wales to rely solely on the pathologist for research? Was not work to be done on live organisms? In defiance of elementary principles of planning the *x*-ray department was so embedded within the building that expansion was wellnigh impossible. A derisory amount of space was allocated for radioisotopes.

Similar lack of anticipation of real needs was shown in the department of mental health, to which space for a trivial 32 beds had been allocated. The grave challenge of mental illness in Wales was once again being evaded by the Cardiff medical college. Through squalid medical politics the college had thwarted for decades the establishment of a chair and department of psychiatry. Despite repeated and recent demands there was still no sign of it. The relegation of psychiatry in this hospital to a Cinderella role was little short of scandalous. If the miserable ancillary space and facilities that were intended were compared with the standards in the Ministry's draft Building Note 5, the importance would be realized of the Minister adding his voice to that of the Minister for Welsh Affairs in calling for a chair and department of psychiatry.

Independent expert opinion in the *Architects' Journal* had declared the design to be medically an antique and

architecturally a disaster; Wales was being offered a second-rate hospital that must not be built. The temperate *British Medical Journal* had spoken of the design as old-fashioned, as embodying many faults, a design where flexibility had been sacrificed to monumental mass, and had bluntly subtitled its editorial on the competition with the heading "Was it worth it?"

Catalogue of Blunders

The most dismaying feature was the ludicrous amount of space allocated for research work in relation to bed space. No one had been more dismayed about this than the University Grants Committee, who wanted the research facilities increased. The present design gave every indication of there having been a battle for beds between heads of departments who had measured their prestige by the number of beds allotted to them, rather than being prompted by a concern that the hospital should be a great teaching centre serviced with extensive research facilities.

In this design for an £8m. hospital blunder after blunder emerged. Quiet-rooms were in the noisiest part of the building. The sluice-room was furthest from the beds most needing its services. Cross-infection risks were increased by infected material being brought into the ward suite for disposal. Lavatories were so sited as to increase the difficulties of early ambulation. The operating theatre was to have a wood-block floor that could never be sluiced clean. Current ideas on ward planning, reducing the maximum to six beds, were not being followed. Day space was insufficient for the intended number of patients. The huge expanse of low building in front of the low block would require constant artificial light. The eight-story light wells for the ward block were contrary to modern practice, and would mean that wards would be badly lit and have a wretched outlook. The prevailing wind would blow smoke from the boilerhouse to the ward block. There was doubt whether there could be extensions without emptying wards in use. Expansion of the out-patients' department would be a most difficult operation. Wales might forgive the blunders, but it would not forgive this hospital, costing the fantastic figure of £10,000 a bed, being built in its present form.

Promoters' Fully Integrated School

Miss PITT stated that the fact that this was to be an undergraduate medical school dictated not only the concept of the work to be performed, but also the site of the hospital, which would have 650 beds. The scheme must be viewed against the development of acute hospital services in South Wales. This would involve another major acute regional hospital in the Cardiff area, major acute hospitals either existing or being provided at Bridgend, Pontypridd, and Newport, and those projected for Merthyr and North Monmouthshire.

Dealing with the points of criticism, she said that the out-patients' department had been conceived in full accord with modern thought, and was to be developed on polyclinic lines with a view to carrying out the maximum amount of investigation and treatment on an out-patient or day-hospital basis. This would avoid unnecessary admissions. Hence the department was slightly larger than would be normally expected in a hospital of this size.

The promoters did not ask for a medical school tacked on to a hospital. They wanted the two together. They required a building in which the department of medicine, with its teaching facilities and research laboratories, formed part of the medical wards, the surgical department with the surgical wards, etc. They considered integration, with the close day-to-day working it would produce, was a progressive concept which would be followed by many others in the future. They foresaw great benefits in care and treatment, the furthering of medical education, and the promotion of research. The scheme provided for over 70 laboratories, of which 40 were specifically allocated to research. In addition to integration of the school departments with the wards, the promoters—because of the dependence of medical units one on another—also required a reasonably compact, complete unit. These fundamental requirements had inevitably tended towards a main building of some bulk. That was the price they were prepared to pay for the fullest development of their ideas.

Replanning in Progress

In the process of development of sketch plans much rearrangement and replanning was being carried out. A series of working parties had been set up to go into the plans of the various units with the architect and the engineer. One instance of this was the internal design and layout of the ward unit. This had already been replanned to provide better access and supervision, and take account of the latest thoughts on cross-infection. More single rooms had been provided, and the large 10-bed unit broken up into smaller units. This was a normal process that would be expected with any design, and similar replanning was going on throughout the hospital. Concentration of the main block had enabled part of the site to be kept clear, leaving room for future building. The principal consideration in the siting of the boilerhouse was thermal efficiency. The possibility of smoke nuisance had not been overlooked; arrangements had been made for a wind-tunnel test, and this might point to the need for a higher chimney or other remedy.

The seven-story light wells—not eight—were 140 ft. by 60 ft. and would allow adequate light. The planning of the ward blocks provided that in the main the bed positions were on the outside walls, and it was the service rooms that faced inwards. It was true that the plan envisaged building at a later stage above wards in use, and that this would be inconvenient. It was outweighed by the alternative disadvantage of having additional ward accommodation in the wrong place. One of the modifications already under consideration was the possibility of completing the ward block at the outset, leaving additional building if required to be carried out elsewhere on the site. The proposed hospital represented a considerable advance. Inevitably hospitals took a long time to design and bring into operation, and with an expanding programme they must be overtaken by new conceptions. This hospital gave the promoters what they wanted. They had examined the design carefully in the light of the numerous criticisms and were satisfied that the completion of detailed sketch plans now in process of preparation would give them a modern and efficient hospital and a medical teaching centre.

LABOUR'S SOCIAL SERVICE TEMPLE

[FROM OUR PARLIAMENTARY CORRESPONDENT]

Mr. HAROLD WILSON (Huyton, Lab.), threatening the Government on November 2 with opposition from a Labour Party united on everything but defence, noted the omission from the Queen's Speech of any reference to the Health Service. They had, he claimed, every right to know what the Government intended. A new Minister of Health had been appointed who, whatever his personal and public qualities—and they were great—was for all that a sworn enemy of the principle of a free and comprehensive health service. He was a sophisticated debater, capable of rationalizing the crude and ignorant prejudices of so many Tory supporters. At the Conservative Party conference he had seemed to commit himself to legislation to bar aliens from using the Health Service. The Service had done more than anything in history to bring healing and security to millions of working and middle-class families for whom in the past serious illness had often meant domestic ruin. "I warn the Tories," he declared, "that if they lay sacrilegious hands on the Health Service, which we regard as the very temple of our social security system, I promise them that the Labour Party will fight them with the same determination as we have brought and are bringing to the fight against the Tory Rent Act." They indicted the Government for its administration of the Health Service, an administration which he feared could only be harsher and more inhumane under the new Minister.

Universities and Colleges

UNIVERSITY OF EDINBURGH

At a Graduation Ceremonial on October 22 the degrees of M.B., Ch.B. were conferred on Louise F. Fairley.

UNIVERSITY OF BIRMINGHAM

Professor H. P. Gilding, Bowman Professor of Physiology and Director of the Department of Physiology, retired on September 30, 1960.

The title of University Senior Clinical Tutor has been granted to Mr. M. J. D. Noble, Consultant Obstetrician and Gynaecologist, Marston Green Maternity Hospital; Mr. R. B. Parker, Consultant Obstetrician and Gynaecologist, Sorrento Maternity Hospital; Mr. S. J. Crews and Mr. K. Rubinstein, part-time Consultant Ophthalmologists, Birmingham and Midland Eye Hospital.

The title of University Research Fellow has been given to the following during the tenure of their present awards or appointments in the University: J. Burgess, M.D., Nuffield Fellow, who is working in the Department of Medicine on problems of cardio-respiratory dysfunction; H. J. Yardley, Ph.D., who is working in the Medical Research Council's unit in the Department of Experimental Pathology for research on the experimental pathology of the skin; and W. H. S. George, M.B., Ch.B., B.Sc., who has been awarded a research grant from the United Birmingham Hospitals Endowment Fund to enable him to work in the Department of Experimental Pathology on problems connected with fluorescent labelling of antibodies.

Dr. C. E. Oxnard and Dr. W. A. Marshall have been appointed Research Fellows in the Department of Anatomy, from August 1, 1960, and October 1, 1960, respectively.

Dr. C. G. Caro resigned from the appointment of temporary Lecturer in Medicine on August 31, 1960, and Dr. R. M. Baddeley, Dr A. D. Barnes, Dr. B. Goodhead, and Dr. J. T. Hobbs from their appointments as temporary Lecturers in the Department of Anatomy on September 30, 1960.

UNIVERSITY OF SHEFFIELD

The following appointments are announced: Dr. J. J. Daly, full-time Research Assistant in Medicine; Mr. S. D. Clarke, full-time Lecturer in Surgery; Dr. Jean L. Baker, full-time Research Assistant in Obstetrics and Gynaecology; Mr. D. G. Taylor, part-time Lecturer in Cardiothoracic Surgery; Mr. A. B. Nutt, part-time Lecturer in Ophthalmic Surgery; Dr. R. S. Morton, part-time Lecturer in Venereal Diseases.

The following members of the academic staff have resigned from the appointments indicated in parentheses: Mr. O. Daniel (Senior Lecturer in Surgery); Dr. D. H. Blakey (Lecturer in Obstetrics and Gynaecology); Dr. A. Bradley (Lecturer in Forensic Medicine); Dr. J. D. S. Hammond (Lecturer in Medicine to Dental Students); and Dr. L. Grimshaw (Lecturer in Psychiatry).

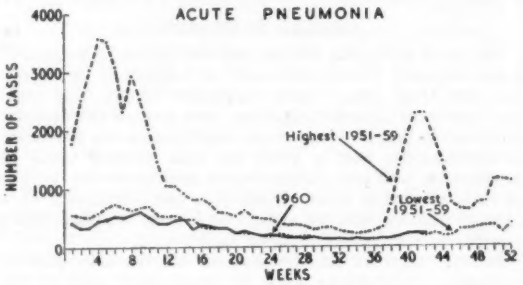
Vital Statistics

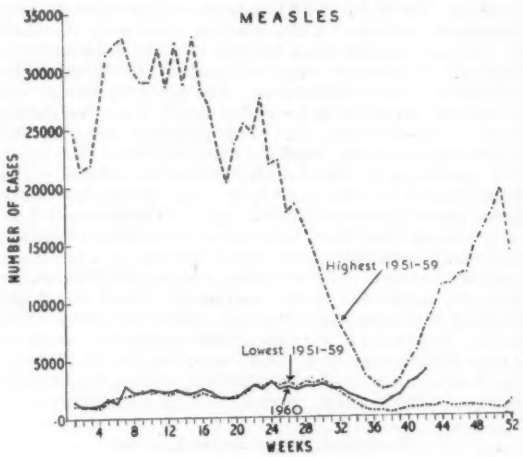
Smallpox in Northern Rhodesia

200 cases of smallpox have been reported in the Luapula Province of Northern Rhodesia in the last four months, and 24 of these have been fatal. The medical officer of health at Fort Rosebery has reported that the majority of these cases had come from the valley of the Luapula River, which forms the boundary between Northern Rhodesia and the Katanga Province of the Congo. The valley is one of the most densely populated areas in Northern Rhodesia, and teams from the Health Department are working in the area vaccinating local tribesmen. In Fort Rosebery itself very few cases have been reported, and all the Europeans there have been vaccinated.—*The Federation of Rhodesia and Nyasaland Newsletter*, October 28, 1960.

Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases of certain diseases notified weekly in England and Wales. Highest and lowest figures reported in each week during the years 1951–9 are shown thus ------, the figures for 1960 thus ———. Except for the curves showing notifications in 1960, the graphs were prepared at the Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.





Infectious Diseases

Areas where the numbers of notifications were high in the latest two weeks for which figures are available.

	Week Ending Oct. 22	Oct. 29
Measles		
Lancashire	1,234	**1,433**
Oldham C.B.	82	**131**
Darwen M.B.	54	**116**
Leigh M.B.	165	**148**
Yorkshire West Riding	401	**474**
Acute Poliomyelitis		
London	4	**3**
Essex	0	**3**
Dysentery		
Sussex	4	**30**
Hastings C.B.	0	**24**
Yorkshire West Riding	56	**101**
Leeds C.B.	29	**64**
Pembrokeshire	3	**31**
Haverfordwest R.D.	2	**26**
Paratyphoid Fever		
Flintshire	0	**5**
Rhyl U.D.	0	**5**
Food Poisoning		
Westmorland	0	**20**
South Westmorland R.D.	0	**20**

INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending **October 22** (No. 42) and corresponding week 1959.

Figures of *cases* are for the countries shown and London administrative county. Figures of *deaths* and *births* are for the whole of England and Wales (London included), London administrative county, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available.

The table is based on information supplied by the Registrars-General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES	1960					1959				
	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire
Diphtheria ..	4	3	1	0	1	6	1	2	0	1
Dysentery ..	465	67	171	14	4	564	58	254	6	5
Encephalitis, acute	2	1		0		8	2		1	
Enteric fever:										
Typhoid ..	4	1	0	0		4	1	2	0	1
Paratyphoid ..	0	0	0	0		8	0	1 (B)	0	1 (B)
Food-poisoning ..	181	25	33	2		179	26	9	0	
Infective enteritis or diarrhoea under 2 years				23	31				28	34
Measles*	3,917	183	80	2	16	1,019	26	28	16	47
Meningococcal infection	19	2	10	1		15	0	10	2	
Ophthalmia neonatorum	31	0	3	0		24	3	4	0	
Pneumonia† ..	213	9	144	3		187	14	141	1	
Poliomyelitis, acute:										
Paralytic ..	10	3	0	0	4	18	2	0	2	
Non-paralytic ..	1	1	0			10	2	0		
Puerperal fever§ ..	188	28	6	0		203	16	13	0	
Scarlet fever ..	465	37	55	23	27	939	48	134	30	41
Tuberculosis:										
Respiratory ..	436	43	83	14		474	59	54	22	
Non-respiratory	59	4	10	2		56	3	13	8	
Whooping-cough	860	81	77	12	44	543	36	115	13	51

DEATHS	1960					1959				
	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire
Diphtheria ..	0	0	0	0	0	0	0	0		0
Dysentery ..	0	0		0		0	0			
Encephalitis, acute		1			0		0			0
Enteric fever ..	0	0	0	0		2	1	0		
Infective enteritis or diarrhoea under 2 years		0	0	1	1	4	0	1		3
Influenza	19	1	0	0	2	19	0	0		0
Measles		0	0	0	0		0	0		0
Meningococcal infection		0	0				0	0		
Pneumonia ..	523	40	15	23	7	373	21	18		7
Poliomyelitis, acute	1	0		0	0	0	0			0
Scarlet fever ..		0	0	0	0		0	0		0
Tuberculosis:										
Respiratory ..	72	4	2	2	2	77	3	2		3
Non-respiratory		0	0	0	0		1	0		0
Whooping-cough	0	0	0	0	0	0	0	0		0
Deaths 0–1 year ..	306	27	14	6	11	269	25	28		10
Deaths (excluding stillbirths) ..	10,111	801	554	127	161	8,383	669	523	111	124
LIVE BIRTHS ..	14,973	1279	1033	284	344	13,620	1182	959	224	368
STILLBIRTHS ..	265	26	22			275	24	28		

* Measles not notifiable in Scotland, whence returns are approximate.
† Includes primary and influenzal pneumonia.
§ Includes puerperal pyrexia.

Medical News

Commonwealth Fund and Harkness Fellowships

The Annual Report of the Commonwealth Fund 1960, an American organization established in 1918—includes details of awards made to Professor R. B. HUNTER (University of St. Andrews) to review developments in selected medical schools in the U.S.A. as an aid in planning for a new medical school and teaching hospital at his own institution, and to Professor D. WHITTERIDGE, F.R.S. (University of Edinburgh) to survey the teaching of physiology and allied preclinical subjects in selected American medical schools and to prepare a report for the Association for the Study of Medical Education in Great Britain. Harkness Fellowships for study in the U.S. were awarded to Mr. R. Y. CALNE, Dr. R. HALL, Dr. G. P. MCNICOL, and Dr. I. C. RODDIE. Of general interest among the grants to American institutions are the endowment of a chair of psychiatry and religion at Union Theological Seminary, and support of a pilot programme at Northwestern University designed to shorten the medical curriculum by two years.

Fulbright Travel Grants

The United States Educational Commission in the United Kingdom announces that, under the provisions of the Fulbright programme, travel grants for 1961 to 1962 are available to citizens of the United Kingdom and dependent territories to go to the United States of America for academic or educational purposes, such as study, research, or lecturing. All awards are competitive and are made by the Board of Foreign Scholarships in Washington upon the recommendations of the Commission. Further details may be obtained from the Commission, 71 South Audley Street, London W.1.

Anaesthetists Dine

On November 4 Sir ARTHUR PORRITT, P.R.C.S., proposed the toast of the Association of Anaesthetists of Great Britain and Ireland at its annual dinner. The president of the association, Dr. R. JARMAN, replied. Dr. R. M. DAVIES proposed the health of the guests, and Mr. ARTHUR BELL, P.R.C.O.G., replied.

Smoking and Chest Disease

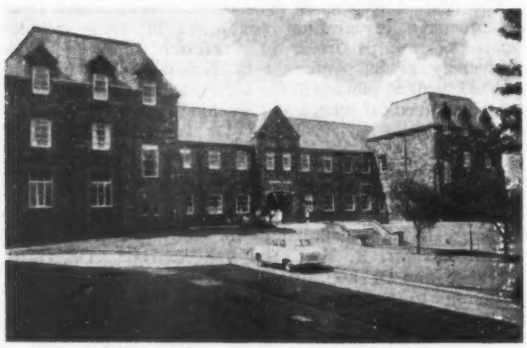
In August this year "Smoking and Chest Disease," a report of the Joint Tuberculosis Council of Great Britain, was published in *Tubercle*, the journal of the British Tuberculosis Association. It was prepared by the Council's committee on smoking, Dr. F. A. H. SIMMONDS, Dr. T. W. DAVIES, and Dr. NORMAN MACDONALD (convener), and reprints are now available (price 1s.) from the Honorary Secretary, Dr. R. L. MIDGLEY, Hawkmoor Chest Hospital, Bovey Tracey, Devon. The report, which was discussed in a *Journal* annotation, October 8, p. 1077, stresses that members of the medical profession should by example and persuasion help their patients and others to reduce or abandon cigarette-smoking.

British Hospitals Contributory Schemes Association

The British Hospitals Contributory Schemes Association made more progress in 1959 than in 1958, according to figures given in their *Twelfth Annual Report, 1959–60*. The total number of contributors in the 37 schemes for which figures could be obtained was only 3,500 short of four million—an increase of 1.76% over 1958, while the total income of more than £3,100,000 showed an increase of 2.6% for the year, compared with 1.6% in 1958. Charitable distributions in 1959 again exceeded £75,000, and brought the total of such distributions during the first 11¼ years of the National Health Service to over £905,000. The B.H.C.S.A. has issued a statement of policy on the provision of convalescent treatment which has been forwarded to the Minister of Health.

Department of Mental Health, Belfast

Windsor House, a century-old building at Belfast City Hospital, has recently been converted for use as a psychiatric unit and department of mental health which will provide Queen's University, Belfast, and the professor of mental health with teaching and research facilities.



Windsor House, Belfast City Hospital.

The department, which has cost £118,000, can house 47 in-patients, and includes an out-patient clinic, as well as treatment facilities, a laboratory specially screened for the use of radioactive isotopes, and departments of psychology and child psychiatry.

Release of Corticotrophin

Corticotrophin will be generally prescribable by the medical profession in Great Britain and Northern Ireland from December 1.

"La Presse Médicale" Film Prize

Applications and films for *La Presse Médicale's* annual prize of 1,000 N.F. for "medico-surgical cinema" should be sent to the Secretariat, *La Presse Médicale*, 120 Boulevard Saint-Germain, Paris 6, France, before February 1. The films must be 16 mm. and must not exceed 30 minutes in length.

Grants, Gifts, and Bequests

The Trustees of the Nuffield Foundation have increased from £60,000 to £100,000 their grant for the erection of the Nuffield Hearing and Speech Centre attached to the Royal National Throat, Nose and Ear Hospital, Gray's Inn Road, London.

The Banting–Best department of medical research in the University of Toronto has been given $1m. by Mr. GARFIELD WESTON, the Canadian industrialist (*The Times*, October 31).

People in the News

Mr. L. FARRER-BROWN, director of the Nuffield Foundation, is to succeed Sir JOHN WOLFENDEN as chairman of the National Council of Social Service.

Dr. T. J. RENDLE-SHORT, lecturer in child health, University of Sheffield, has been appointed to the newly established chair of child health in the University of Queensland, Australia.

Lord MOYNIHAN has been appointed chairman of the North-West Metropolitan Regional Hospital Board.

Dr. MARK WEBSTER, director of medical services in Northern Rhodesia, has been awarded a World Health Organization Fellowship to study hospital services overseas.

Sir ARTHUR MACNALTY has been elected a vice-president of the British Leprosy Relief Association. He was chairman of its medical committee for thirteen years.

COMING EVENTS

Harveian Society and Osler Club.—Joint meeting, November 16, 8.15 p.m., 11 Chandos Street, London W.1.

Heberden Oration.—Dr. J. J. BUNIM (National Institute of Health, Bethesda, Maryland, U.S.A.), "A Broadened Spectrum of Sjögren's Syndrome and its Pathogenetic Implications," December 2, 4.15 p.m., Wellcome Foundation Lecture Hall, Euston Road, London N.W.1.

29th Stephen Paget Memorial Lecture, Research Defence Society.—Professor J. H. BURN, F.R.S., "Testing Drugs on Man," December 6, 5.30 p.m., Physiology Lecture Theatre, University College, London, Gower Street, London, W.C.1. Annual general meeting of the Society after lecture.

Nutrition Society.—Symposium, "Caloric Balance in Man," December 17, Middlesex Hospital Medical School, London W.1. Chairman: Sir CHARLES DODDS, F.R.S. Details from Miss D. F. HOLLINGSWORTH, c/o Ministry of Agriculture, Fisheries and Food, Great Westminster House, Horseferry Road, London S.W.1.

Central Council for Health Education. — Annual conference: "The Road to Maturity," January 26, 10.30 a.m. to 4 p.m., National Film Theatre, South Bank, London S.E.1. Details from C.C.H.E., Tavistock House North, Tavistock Square, London W.C.1. (EUS. 3341.)

Refresher Course in Ophthalmology.—February 20–24, at the Courage Laboratory of the Royal Eye Hospital, with visits to Maida Vale and to the Royal College of Surgeons. Consultant ophthalmologists wishing to attend should write to Professor ARNOLD SORSBY, the Courage Laboratory, the Royal Eye Hospital, St. George's Circus, London S.E.1.

Ophthalmological Society of United Kingdom.—Annual congress, April 13–15, Royal Society of Medicine, 1 Wimpole Street, London W.1. Discussion: "Neovascularization in Ocular Disease." 1961 Bowman Lecture: Miss IDA MANN (Perth, Australia), "Climates, Cultures, and Eye Diseases." Details from Mr. REDMOND SMITH, of the Society, 47 Lincoln's Inn Fields, London W.C.2.

NEW ISSUES OF SPECIALIST JOURNALS

The journals listed below are obtainable from the Publishing Manager, B.M.A. House, Tavistock Square, London W.C.1

BRITISH JOURNAL OF OPHTHALMOLOGY

Strabismic Amblyopia. P. Matteucci.
Retinal Vein Occlusion and Glaucoma. S. Vannas and A. Tarkkanen.
Abiotrophic Ophthalmoplegia Externa. S. I. Davidson.
A Possible Aetiology for Glaucoma in Negroes. M. H. Luntz and R. Smith.
Changes in the Electro-Oculogram Potential Level. Jean R. Davis and B Shackel.
Aberrant Intra-Ocular Lacrimal Gland Tissue. W. S. Hunter.
A New Operation for Glaucoma. F. Sanchez Peña.
Intra-Corneal Lamellar Keratoplasty. T. Krwawicz.
Transcleral Division of Mid-Vitreous Membrane under Visual Control. I. C. Michaelson.
Muscle Transplantation after a Complete Severance of the Medial Rectus Muscle. Oey-Khoen Lian.
Multiple Epithelomata of the Eyelids of One Eye. A. Lister and V. M. Dalley.
Reviews.
Notes.

Volume 44, No. 10. (Monthly; £6 annually. With *Ophthalmic Literature* and Index; £9.)

ANNALS OF THE RHEUMATIC DISEASES

Immunological Aspects of Rheumatoid Disease: A Review. L. E. Glynn and E. J. Holborow.
"Rheumatoid Arthritis" with Negative Serological Reaction. A. St. J. Dixon.
Early Diagnosis of Arthritis of the Hand. E. A. Kauffmann and R. Finlayson.
Observations on the Ultracentrifugal Pattern of Serum Proteins in Rheumatoid Arthritis. Luigi Villa, Angelo Fasoli, Franco Salteri, and Camillo B Balsabio.
Chloroquine in Rheumatoid Arthritis. A. Freedman and V. L. Steinberg.
Clinical Trial of the Therapeutic Value of Certain Antirheumatic Drugs. P. van der Meer and S. A. den Oudsten.
Intra-articular Therapy in Osteo-arthritis. V. Wright, G. N. Chandler, R. A. H. Morison, and S. J Hartfall.
Rheumatic Fever in the Young Adult. J. S. Malpas and J. Landon.
Spiro-ergometry in Patients Suffering from Bechterew's Disease. G. J. van Weerden, S. A den Oudsten, A. L. de Groot, and W. van der Veere.
Inactivation Test of the Lupus Erythematosus (L.E.) Plasma Factor. George Bencze.
Book Reviews.
Australian Rheumatism Association.
Sociedad Mexicana de Reumatologia.
Royal College of Physicians of London.
Abstracts.

Volume 19. No. 3. (Quarterly; £3 annually.)

SOCIETIES AND LECTURES

A fee is charged or a ticket is required for attending lectures marked ●. Application should be made first to the institution concerned.

Monday, November 14

INSTITUTE OF DERMATOLOGY.—5 p.m., Dr. P. D. Samman: Eccrine and Apocrine Glands in Health and Disease.

POSTGRADUATE MEDICAL SCHOOL OF LONDON.—4 p.m., Dr. Brian Ackner: Depressive Illness—Clinical Syndrome and Treatment.

ST. ANDREWS UNIVERSITY.—At Demonstration Room, Department of Medicine, 4 p.m., Mr. W. F. Walker: Surgical Influence on Gastric Physiology.

Tuesday, November 15

BRITISH POSTGRADUATE MEDICAL FEDERATION.—At London School of Hygiene and Tropical Medicine, 5.30 p.m., Dr. K. S. Kirby: Nucleic Acids and Cancer.

●INSTITUTE OF OBSTETRICS AND GYNAECOLOGY.—At Hammersmith Hospital, 3 p.m., Dr. H. Payling-Wright: Varicose Veins in Pregnancy.

LEEDS NEUROLOGICAL SCIENCES COLLOQUIUM, 1960.—At Littlewood Hall, General Infirmary at Leeds, 5.15 p.m., Dr. Bertram Selverstone (U.S.A.): Modern Treatment of Gliomas.

MANCHESTER MEDICAL SOCIETY: SECTION OF MEDICINE.—At Large Anatomy Theatre, Manchester University Medical School, 4 for 4.30 p.m., Dr. J. J. Bunim (Maryland, U.S.A.): Alkaptonuria and Ochronosis.

ST. MARY'S HOSPITAL MEDICAL SCHOOL.—At Lecture Theatre, Wright-Fleming Institute, 5 p.m., Professor Norman Morris: Human Relations in Obstetrics.

UNIVERSITY COLLEGE LONDON: DEPARTMENT OF PHARMACOLOGY.—At Physiology Theatre, Gower Street, W.C., 5.30 p.m., public lecture by Professor J. H. Gaddum, F.R.S.: Pharmacological Analysis of Tissue Extracts.

WEST END HOSPITAL FOR NEUROLOGY AND NEUROSURGERY.—5.30 p.m., Mr. G. C. Knight: Trigeminal Neuralgia.

Wednesday, November 16

BIRMINGHAM MEDICAL INSTITUTE: MIDLAND MEDICAL SOCIETY SECTION.—At Birmingham Accident Hospital, 8.30 p.m., clinical meeting. Mr. W. Gissane: Some Medico-social Problems with Injuries in Old People; Mr. P. S. London: Some Problems in Resuscitation, Diagnosis and Treatment of Multiple Injuries; Mr. J. H. Hicks: The Place of Internal Fixation in the Treatment of Fractures.

HARVEIAN SOCIETY OF LONDON.—At 11 Chandos Street, W., 8.15 p.m., joint meeting with Osler Club. Dr. A. White Franklin: History of the Osler Club; Dr. Maurice Long: History of the Harveian Society; Dr. T. F. Cotton: Gibson's "Lost Manuscript"; Sir Geoffrey Keynes: Portrait of William Harvey; Mr. A. Dickson Wright: Harvey and Osler.

INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. H. Haber: Clefts, Vesicles, and Bullae.

INSTITUTE OF DISEASES OF THE CHEST.—5 p.m., Dr. J. N. Pattinson: Some Abnormalities of the Mediastinum.

INSTITUTE OF UROLOGY.—4.30 for 5 p.m., Mr. D. E. H. Phillips: Implantation of the Ureter.

●LEEDS UNIVERSITY.—At General Infirmary at Leeds, (1) 5 p.m., Mr. G. W. Theobald: Gynaecological Pain. (2) 6 p.m., Mr. J. B. Farquhar: Third Stage of Labour.

POSTGRADUATE MEDICAL SCHOOL OF LONDON.—2 p.m., Dr. A. L. Greenbaum: Fat Metabolism.

ROYAL FREE HOSPITAL, Gray's Inn Road, London W.C.—5.15 p.m., Sir William Morrow (Sydney): Ulcerative Colitis.

ST. ANDREWS UNIVERSITY.—At Demonstration Room, Department of Medicine, 2.30 p.m., Mr. W. F. Walker and Dr. H. G. Morgan: Electrolyte Disturbances from Abdominal Operations.

Thursday, November 17

BRITISH INSTITUTE OF RADIOLOGY.—8 p.m., Mr. J. B. Massey, Mrs. J. J. Gough, Dr. W. Shanks, and Dr. A. M. Jelliffe: The Role of Moving Field Techniques in Treatment with High Energy Radiation.

BRITISH POSTGRADUATE MEDICAL FEDERATION.—At London School of Hygiene and Tropical Medicine, 5.30 p.m., Dr. J. C. Kendrew: Structure of Proteins.

GUTHRIE SOCIETY.—At Westminster Hospital Medical School, 8 p.m., Mr. P. H. Addison: Legal Pitfalls of Medical Practice.

HUNYMAN GILLESPIE LECTURES.—At Anatomy Theatre, University New Buildings, Teviot Place, Edinburgh, 5 p.m., Professor T. N. A. Jeffcoate: Functional Disorders of the Female Bladder and Urethra.

LIVERPOOL MEDICAL INSTITUTION.—History of Medicine Lecture by Dr. W. S. C. Copeman: Elizabethan Medical Students.

MANCHESTER MEDICAL SOCIETY.—At Large Anatomy Theatre, Manchester University Medical School, 7.30 for 8 p.m., meeting of Fellows arranged by Section of Anaesthetics: Sir Robert Macintosh: A Trip to Russia and China.

NUFFIELD ORTHOPAEDIC CENTRE.—At Wingfield-Morris Orthopaedic Hospital, Oxford, 8.30 p.m., Mr. J. Crawford Adams: Ischio-femoral Arthrodesis for Osteoarthritis and Tuberculous Arthritis of the Hip.

ROYAL COLLEGE OF PHYSICIANS OF LONDON.—5 p.m., Langdon-Brown Lecture by Dr. D. V. Hubble: The Endocrine Orchestra.

ROYAL SOCIETY OF TROPICAL MEDICINE AND HYGIENE.—At Liverpool School of Tropical Medicine, Pembroke Place, Liverpool, 7.30 p.m., laboratory meeting. Demonstrations.

ST. ANDREWS UNIVERSITY.—At Physiology Department Lecture Theatre, Queen's College, Dundee, 5 p.m., Mr. L. N. Pyrah: Use of the Loops of Small and Large Intestine in Urological Surgery.

ST. GEORGE'S HOSPITAL MEDICAL SCHOOL.—5 p.m., Dr. Desmond Curran: postgraduate demonstration in psychiatry.

SOCIETY OF MEDICAL OFFICERS OF HEALTH: HOME COUNTIES BRANCH.—At Room 105, London School of Hygiene and Tropical Medicine, 3 p.m., Dr. G. S. Wigley: Mental Health Act—An Administrator's View.

Friday, November 18

BIOCHEMICAL SOCIETY.—At Middlesex Hospital Medical School, 10 a.m., 400th meeting. Colloquium on Histochemistry.

FACULTY OF RADIOLOGISTS.—At Royal College of Surgeons of England, 4.30 p.m., 25th Skinner Lecture by Professor R. W. Scarff: Prognosis in Carcinoma of the Breast.

GALENICALS.—At Royal Fort, Bristol, 5.30 p.m., Honorary Presidential Address by Dr. R. E. Hemphill: Psychological Disorder and the Artist.

●INSTITUTE OF DERMATOLOGY.—5 30 p.m., Dr. I. Muende: clinical demonstration.

INSTITUTE OF DISEASES OF THE CHEST.—5 p.m., Dr. J. Smart: clinical demonstration.

LONDON UNIVERSITY.—At Anatomy Theatre, University College, 5.30 p.m., special university lecture by Professor M. Westergaard (Copenhagen): Some Fundamental Concepts and Problems in Molecular Genetics.

PLYMOUTH MEDICAL SOCIETY.—At South Devon and East Cornwall Hospital, Freedom Fields, 8.30 p.m., joint meeting with Plymouth Division, B.M.A. Lecture by Dr. Richard Asher: See How They Come.

POSTGRADUATE MEDICAL SCHOOL OF LONDON.—(1) 10 a.m., Mr. H. Osmond-Clarke: Cervical Disk Lesions. (2) 4 p.m., Professor C. E. Dent: Primary Hyperparathyroidism.

ROYAL MEDICO-PSYCHOLOGICAL ASSOCIATION.—At Barnes Hall, Royal Society of Medicine, 2.15 p.m., 35th Maudsley Lecture by Dr. Eliot Slater: Hysteria 311.

ST. ANDREWS UNIVERSITY.—At Demonstration Room, Department of Medicine, 4 p.m., Dr. J. A. R. Lenman: Investigation of Cerebral Circulation.

APPOINTMENTS

EAST ANGLIAN REGIONAL HOSPITAL BOARD.—G. H. Day, M.D., Consultant Physician/Superintendent, Mundesley Hospital; M. A. Pears, M.D., M.R.C.P., Consultant Physician, King's Lynn Hospital Group; I. McKechnie, F.R.C.S.Ed., Consultant Orthopaedic Surgeon, Peterborough and Stamford Hospital Group; A. T. Lloyd, M.B., Ch.B., D.P.M., Senior Registrar in Psychiatry, Fulbourn and Addenbrooke's Hospitals; N. A. Blumberg, M.B., Ch.B., F.R.C.S., Surgical Registrar, Ipswich and East Suffolk Hospital; J. S. Mehta, M.B., B.S., Radiological Registrar, Ipswich and East Suffolk Hospital; I. Varsamis, M.B., B.Ch., Registrar in Psychiatry, St. Andrew's Hospital, Norwich; Sheila J. Wallace, M.B., B.S., D.Obst.R.C.O.G., Paediatric Registrar, Ipswich and East Suffolk Hospital; M. S. Banerjee, M.B., B.S., D.G.O., Registrar in Obstetrics and Gynaecology, Norfolk and Norwich Hospital Group; G. C. L. Goss, M.Sc., Ph.D., M.B., B.S., Registrar in Psychiatry, Hellesdon Hospital.

ENOCH, MORGAN D., M.R.C.S., L.R.C.P., D.P.M., Senior Hospital Medical Officer, Runwell Hospital, Wickford.

HOSPITAL FOR SICK CHILDREN, Great Ormond Street, London, W.C.—E. Sheville, M.B., Ch.B., D.M.R.D., Registrar in Radiology; S. Sarkar, M.B., D.L.O., Senior Ear, Nose, and Throat Registrar; H. R. Dingle, B.M., B.Ch., D.A., Resident Anaesthetic Registrar, Tadworth; Dorothy E. Harris, M.B., B.S., F.F.A.R.C.S., Junior Resident Anaesthetist; L. W. Lowe, M.B., Ch.B., House-surgeon; Anne A. Ferry, M.B., B.S., L. Stimmler, M.B., B.S., M.R.C.P., and K. E. Scott, M.D., C.M., House-physicians; E. Aberdeen, M.B., B.S., F.R.C.S., D.C.H., Surgical First Assistant to the Cardiothoracic Unit.

LIVERPOOL REGIONAL HOSPITAL BOARD.—D. N. Edwards, M.B., B.S., D.M.R.T., and H. J. Hughes, M.B. B Ch., D.M.R.T., Whole-time Assistant Radiotherapists with Regional Radiotherapy Service; J. W. B. Forshaw, M.D., M.R.C.P., Whole-time Consultant Physician and Deputy Medical Superintendent of Sefton General Hospital; C. A. Hopkins, M.B., Ch.B., M.R.C.P., Whole-time Consultant Chest Physician and Deputy Physician Superintendent of Aintree Hospital; K. M. Fraser, M.B., Ch.B., D.C.H., D.P.M., Consultant in Child Psychiatry, and J. Rees Roberts, M.D., M.R.C.P., Part-time Consultant Paediatrician in Neurology, both to Alder Hey Children's Hospital.

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

Clayton.—On October 24, 1960, at Redhill County Hospital, Redhill, Surrey, to Pamela (formerly Passmore), M.B., B.S., D.A., and Major Peter Clayton, M.B.E., a sister for Patrick—Gillian Barbara.

Davis.—On October 10, 1960, at 9 Forrest Gardens, Norbury, London S.W., to Margaret (formerly Liddle), S.R.N., and Leslie R. Davis, M.D., a daughter—Belinda Joy.

Macnamara.—On October 29, 1960, to Margaret, wife of Dr. B. G. P. Macnamara, of 109 King's Avenue, London S.W., a daughter—Fiona Maria.

MARRIAGES

Long—Irwin.—On October 22, 1960, in London, Merton Long, M.B., Ch.B., of Harlow, Essex, to Patricia Irwin, S.A.N., S.C.M., of Hull, Yorks.

Wand—Crew.—On November 2, 1960, in London, Solomon Wand, M.B., Ch.B., Hon.D.C.L., of Birmingham, Warwicks, to Shaunagh Denison Crew, S.R.N., S.C.M., of Milford-on-Sea, Hants.

DEATHS

Cumberlege.—On October 26, 1960, in a nursing-home, Clifton, Bristol, Gilbert Iliffe Cumberlege, M.D., formerly of Cardiff.

Elliston.—On October 24, 1960, in Noble's Hospital, Douglas, Isle of Man, Chatterton Eric Elliston, M.D., aged 78.

Hacker.—On October 24, 1960, in hospital, F. Alfred Risdon Hacker, M.R.C.S., L.R.C.P., Lieutenant-Colonel, R.A.M.C., retired, of Fairhaven, Brockenhurst, Hants.

Hastings.—On October 25, 1960, in a nursing-home, William Howitt Hastings, M.B., B.Ch., D.M.R.E., Surgeon Captain, R.N., retired, of 2 Strathmore Court, East Parade, Bexhill-on-Sea, Sussex, aged 81.

Henderson.—On October 25, 1960, at his home, John Henderson, M.B., Ch.B., M.R.C.O.G., of Edgehill, Castlehead, Paisley, Renfrewshire, aged 36.

John.—On October 12, 1960, Harold Griffiths John, M.R.C.S., L.R.C.P., of Leek Road, Weston Coyney, Stoke-on-Trent, Staffs, aged 53.

Lillie.—On September 26, 1960, in hospital, Hubert Jack Lillie, M.B., Ch.B., of "Hillside," Cleobury Road, Bewdley, Worcs.

Macbeth.—On October 14, 1960, in a nursing-home, Edinburgh, John Stewart Macbeth, M.B., Ch.B., D.P.H., of the Schoolhouse, Cremerston, Berwick-on-Tweed.

MacDonald.—On October 13, 1960, at Gutach-Breisgau, Germany, George Allardice MacDonald, M.B., C.M., of Clarens-Montreux, Switzerland, aged 91.

Michell.—On October 16, 1960, Charles Francis Michell, M.B., B.S., of 199A Coldharbour Lane, London S.E.

Patrick.—On October 18, 1960, Henry Forbes Patrick, M.R.C.S., L.R.C.P., F.F.A. R.C.S., of Little Knoll, West Chiltington, Pulborough, Sussex.

Popper.—On October 13, 1960, Erwin Popper, M.D.

Ridley.—On October 19, 1960, at 39 Saxon Road, Hastings, Elsie Emma Alice Ridley, M.D., formerly of Hove and Patcham, Sussex.

Stronach.—On September 14, 1960, Ronald Douglas Stronach, M.B., F.R.C.S.Ed., of Palmerston, Otago, New Zealand.

Wood.—On October 14, 1960, at the Royal Masonic Hospital, Albert William Wood, M.R.C.S., L.R.C.P., of Ferndown, Dorset.

Any Questions ?

We publish below a selection of those questions and answers which seem of general interest. It is regretted that it is not possible to supply answers to all questions submitted.

High-protein Diet in Myopia

Q.—*Will a high-protein diet prevent the progression of myopia? If so, is such a diet feasible?*

A.—There is some evidence[1] that myopia progresses more in children who are growing fast and who do not like some protein-containing foods. Although this evidence is not conclusive, and it does not necessarily follow that a high-protein diet will prevent the progression of myopia, it seems worth attempting to supplement the diet of such children with animal protein. The feasibility of such a diet depends mainly on the social circumstances. Foods containing first-class protein are expensive and it may be difficult to arrange special diets for children at boarding school.

REFERENCE

[1] Gardiner, P. A., *Brit. med. J.*, 1956, **2**, 699.

Chlorine in Public Water Supply

Q.—*What is the maximum concentration of chlorine in potable water supplied by a public authority, and can chlorine at such concentration be detected by smell and/or taste? Are there any toxic effects from drinking chlorinated water at the optimum concentration or if this is exceeded within likely limits?*

A.—The question as it stands is very difficult to answer since it presupposes that there is such a thing as a simple "optimum" or a "maximum" concentration of chlorine in a public water supply. The purpose of chlorination is threefold: (1) disinfection—i.e., the production of a water which is safe to drink but which is not necessarily sterile in the bacteriological sense, as bacterial spores are unaffected; (2) improvement in the appearance of the water by the oxidative action of chlorine on foreign colouring matter, and (3) removal of certain unpleasant tastes apt to be present in untreated water, chiefly derived from decomposition products of plants, including algae. The amount of chlorine necessary to achieve these ends depends on a large number of factors such as the degree of bacterial contamination of the untreated water; the amount of organic matter, in particular ammonia, present in the untreated water; and the temperature and *p*H of the untreated water. These factors vary to a large extent depending on the source of the water being treated—e.g., spring, shallow or deep well, upland surface water, or a river-derived supply—and, in turn, these will be influenced by the geology and topography of the area of the source.

The amount of chlorine necessary to produce a water which can be relied upon as safe to drink will also depend upon the particular purification process employed at the works; for example, whether slow sand, rapid, or dual filtration are used, whether any coagulant is added for the removal of suspended matter, whether the water is softened, whether terminal ammoniation to "fix" the residual of free chlorine is applied, or if superchlorination followed by dechlorination by means of sulphur dioxide or sodium thiosulphate is utilized. The amount of chlorine necessary will also depend on the particular stage in the purification process at which it is applied and the "contact time" available, that is to say, the period during which the chlorine can act before the water is pumped into the distribution system.

There are thus a multitude of factors to be considered, and space permits only the mention of a few. In general the optimum concentration of chlorine might be defined as that providing the maximum degree of security with the minimum inconvenience due to chlorinous taste. This can be determined for any particular supply only empirically, by frequent taste and bacteriological tests, as even the water derived from the same source is apt to vary according to meteorological conditions, the amount being abstracted, etc.

Sensitivity to chlorinous taste varies enormously among individuals and also apparently from area to area. It has been found that in London the public cannot generally detect chlorine in a concentration of less than 0.1 mg./litre. There are, however, certain persons with unusually sensitive palates who can detect chlorine in less than this amount.[1] No toxic effects upon human beings have ever been substantiated due to drinking water containing the amounts of residual chlorine found after normal waterworks purification processes. For further information the inquirer is advised to consult *The Examination of Waters and Water Supplies*.[2]

REFERENCES

[1] Taylor, E. W., 38th Report on the results of bacteriological, chemical, and biological examination of the London waters for the years 1957-1958. Metropolitan Water Board, p. 90.

[2] Thresh, J. C., Beale, J. F., and Suckling, E. V., revised, Taylor, E. W., *The Examination of Waters and Water Supplies*, 1958. J. and A. Churchill, London.

Tendency to Allergic Reactions

Q.—*A patient is sensitive to serum and to penicillin. Is there a common factor linking these reactions?*

A.—The common factor linking these reactions is the patient. He has the tendency to develop allergic reactions, as occurs in some 10% of the population. Serum and penicillin have no common allergen, but each one is well-known to have allergenic properties. The patient's story serves to remind us that penicillin has replaced foreign serum as the commonest cause of anaphylactic reactions. Allergic reactions to both are commonly urticarial in type.

NOTES AND COMMENTS

Excluding Noise.—Dr. C. G. EASTWOOD (Cambridge) writes: In answer to a question ("Any Questions?" September 24, p. 958) various ear-plugs are recommended. No mention is made of wax ear-plugs. I can strongly recommend those made by Boots Pure Drug Company. They are sold in boxes of half a dozen pink balls of wax which, when softened a little by the warmth of the hand, may be moulded to fit the ear. They exclude almost all sound and appear to have no disadvantages or injurious effects.

OUR EXPERT replies: The wax ear-plugs made by Messrs. Boots are, of course, well known. However, while they are satisfactory for use in certain industries, I do not recommend them for noise abatement in aircraft for the simple reason that the wax is inclined to fit too well, thus forming a plug which is exposed and likely to react to changes in barometric pressure. In fact, I know two instances when their use has caused severe pain and some barotrauma due to their contact with the tympanum.

Correction.—In the article entitled "Dexamethasone Myopathy" (October 15, p. 1129) by Drs. D. N. Golding and T. B. Begg the normal urinary creatinine excretion was wrongly printed as 100 mg. in 24 hours instead of 1,000 mg.

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